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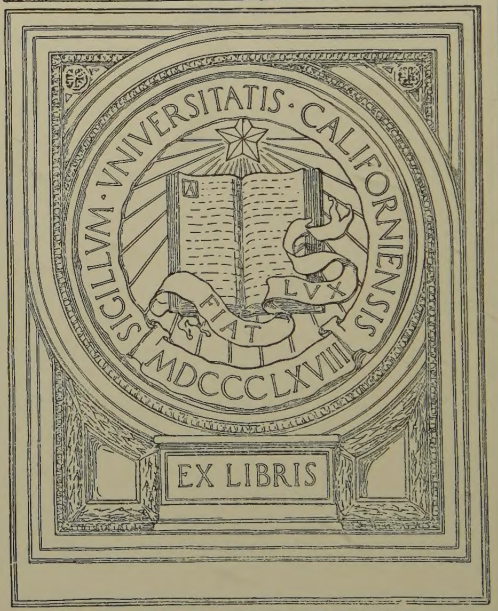

DISEASES OF CHILDREN

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CHAPTER XXIII

RHEUMATISM

WILFRID SHELDON

Nomenclature.—Rheumatism has become a household word to cover a great variety of symptoms both in adults and children, symptoms which often have little or no connection with the acute rheumatism of childhood. Thus lumbago, sciatica, fibrositis and the innumerable aches and pains in the limbs of children are often spoken of as "rheumatic." This has led to much confusion, and may well make one wonder whether the word rheumatism does really represent a clearly defined clinical picture. Even a rheumatic tonsillitis has been supposed, although there is at present no way of foretelling whether an attack of tonsillitis will or will not be followed by manifestations of acute rheumatism.

In an attempt to demarcate the rheumatic manifestations of childhood, Miller introduced the term "juvenile rheumatism" to cover rheumatic heart disease, acute polyarthritis, pains in the limbs, and chorea, and this term is often used in this country. Meanwhile the conception of rheumatic fever, which originally was used simply to indicate acute rheumatic polyarthritis, has extended. A century ago, Bouillaud (1840) emphasized the great frequency of cardiac involvement in rheumatic fever. The close connection between subcutaneous nodules and rheumatic infection was pointed out by Meynet (1878), and that the same process was at work in the production of both nodules and rheumatic carditis was stressed by Barlow and Warner (1881). Romberg (1894) and Poynton (1899) described multiple foci of interstitial inflammation in the heart, and in 1904 Aschoff recognized the specific rheumatic nature of these submiliary foci in the heart muscle. In much of the foreign literature of the present day, the term rheumatic fever embraces both rheumatic polyarthritis and rheumatic heart disease. The view that rheumatic fever represents the response of the body to an infecting agent is now widely accepted, and attempts have been made to separate this disease from other so-called rheumatic conditions by giving it such names as "infectious rheumatism" and "rheumatic granulomatosis." In this chapter, the expression "acute rheumatism" will be used to cover acute rheumatic polyarthritis and rheumatic disease of the heart, including subcutaneous nodules. The other common rheumatic condition in children, namely chorea, will also be described. Whilst there can be no doubt of the close clinical bonds which associate chorea with acute rheumatism, it remains to be proved that there is a common pathological process underlying these two conditions. With further knowledge, it may be that an identical mechanism will be found at work in the production of both chorea and acute rheumatism; meanwhile their clinical affinity certainly warrants the term "rheumatic chorea."

Incidence.—Acute rheumatism is one of the most common and most serious of the diseases of childhood. Before the 1939 war, in the medical wards of The Hospital for Sick Children, Great Ormond Street, 20 per cent. of the beds were constantly occupied by rheumatic children. The seriousness of acute rheumatism lies in the fact that it is the predominating cause of organic heart disease. Acute rheumatism is not a notifiable disease, and therefore its actual incidence is difficult to ascertain, but there is no doubt that it is on the wane. In 1852, 11·2 per cent. of all admissions to London hospitals were for acute rheumatic polyarthritis, a figure which by 1914 had fallen to 5 per cent. The crude death-rate per million persons from rheumatic fever fell steadily from 67 in 1901 to 48 in 1913 and to 12 in 1942. The percentage of London elementary school children found by school doctors to be suffering from cardiac disease, the number inspected annually being about 280,000, declined steadily year by year from 2·1 per cent. in 1923 to 0·68 in 1938.

Ætiology.—*Distribution.*—Although acute rheumatism is of world-wide distribution, it is particularly a disease of the temperate zones. Clarke (1930) has brought forward evidence that it is from 15 to 20 times more common in Europe than in the tropics. Whether any particular racial type is peculiarly prone to rheumatic infection is uncertain. Whilst some investigators have considered that the blonde Nordic types are more often attacked than those with a dark Iberian ancestry, others have been led to the opposite conclusion. Red-headed children have also been dubbed as especially likely to be rheumatic subjects, but the author was unable to confirm this from the material at the rheumatism clinic at Great Ormond Street. With regard to locality, the disease is undoubtedly more prevalent in the big cities than in country districts, and in this connection a great variety of factors, such as poverty, overcrowding, bad sanitation, poor ventilation, dietetic insufficiencies, and dampness each probably play their part. These various factors have their origin in poverty, and much has been made of the fact that acute rheumatism is principally a disease of the poorer classes. Although this is true, it must be remembered that acute rheumatism does occur in the children of the well-to-do. Whether or not the incidence is as great in the thoroughly poor as it is in the artisan class has been questioned; reliable figures on this point are difficult to ascertain, and there is no good evidence that the incidence of acute rheumatism tends to abate in the more severe grades of poverty.

Climate and soil.—Both climate and the type of soil have been thought for many years to be connected with rheumatism. There is a close association between the occurrence of pains in the limbs in children (growing pains) and damp weather, particularly when after a period of warm weather a wet spell suddenly supervenes, and in this country acute rheumatism flourishes most strongly during the cold wet months. Gravel soils which drain quickly are to be preferred to clay, but provided that proper drainage can be obtained, the type of soil probably exerts only a small influence.

Diet.—There are no particular food-stuffs which have been shown to

be detrimental to rheumatic children, and diet plays no important part in the ætiology of acute rheumatism except in the sense that a generous well-balanced diet increases the child's resistance against infections.

Heredity.—The influence of heredity as a factor in the production of acute rheumatism is difficult to assess. Certainly a history of "rheumatism" is common enough in the parents, uncles and aunts of rheumatic children, and it is also frequently found that more than one child in a family is the subject of rheumatic infection. But it is at least as likely that the various adverse environmental circumstances in which rheumatic families usually live play as important a part in the family incidence as does a direct hereditary influence. There may even be a common source of infection for all the children of a family, as was suggested some years ago by Swift, who learned that the mother of one of his rheumatic children frequently had a sore throat within a short time of the appearance of a rheumatic relapse in the child. Following the removal of badly diseased tonsils from the mother, her sore throats ceased, and thereafter the child was free from recrudescences of rheumatism.

If, however, the view that acute rheumatism is the outcome of an abnormal immune response to infection (streptococcal) eventually proves correct, it will still remain to explain why only a small proportion of children experiencing such infection respond by developing a rheumatic reaction. It may well be that this abnormality is to some extent an inherited defect.

Age.—The age incidence of acute rheumatism is one of the striking features of the disease. Poynton has recorded an instance of rheumatic chorea at ten months, and both chorea and rheumatic heart disease have been encountered as early as the second year. The disease is, however, rare before three years of age, and is uncommon under five. In fact so rare is rheumatism under three years, that one would properly hesitate before making the diagnosis at that age. After the fifth year, the incidence rises rapidly to reach its maximum between the eighth and tenth years. The number of first attacks and of relapses steadily declines after puberty.

Whatever the pathogenesis of acute rheumatism may eventually prove to be, this peculiar age incidence will call for an explanation. Although the age incidence coincides with the period of schooling, this is probably of little importance except as regards chorea. Children affected by chorea are generally bright and intelligent, just those to be selected for higher examinations and scholarships, and a history of such extra mental effort not uncommonly foreruns the appearance of choreic movements.

Sex.—Roughly three girls are affected for every two boys. The heavier incidence among girls is largely accounted for by the greater number of cases of chorea which they furnish. Rheumatic heart disease is only slightly commoner among girls.

Relation to other diseases.—It has long been known that there exists a close relation between acute tonsillitis and the onset of rheumatism.

At the end of the last century Haig-Brown pointed out that there was usually an interval between the tonsillitis and the development of rheumatism, and Schlesinger (1930) and the author (1931) have emphasized the importance of this interval, which lies between ten and twenty-one days. During this interval the child is seemingly well. The sore throat varies considerably in severity, sometimes amounting to no more than 2 or 3 degrees of fever for twenty-four hours, and with no complaint by the child, but examination shows reddening and injection of the fauces. Such a condition must often pass unnoticed and the child continue to attend school. On the other hand, there may be a brisk follicular tonsillitis with purulent exudate. The type of infection which quickly penetrates to the cervical glands, causing acute inflammation in them, is less likely to be followed by rheumatism. The modern conception of an

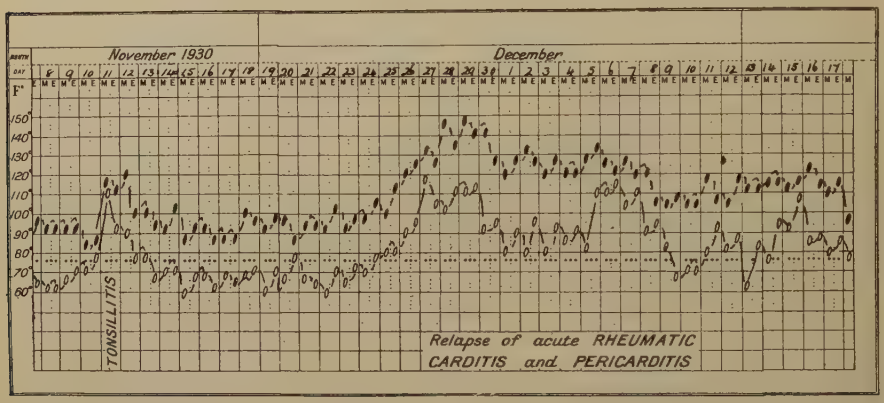

FIG. 324.—TEMPERATURE AND PULSE CHART ILLUSTRATING THE INTERVAL BETWEEN TONSILLITIS AND AN ENSUING RELAPSE OF ACUTE RHEUMATISM.

From a girl aged six years, who on admission to hospital had an enlarged heart with loud mitral murmurs, but no evidence of active disease. On 11.11.30 she had acute follicular tonsillitis, from which a swab grew a pure growth of hæmolytic streptococci. Sixteen days later she developed a fresh outburst of acute rheumatic carditis with pericarditis, and eventually died five months later from progressive cardiac failure.

attack of acute rheumatism may be said to date from the sore throat rather than from the subsequent rheumatic manifestation, and when the pathological relationship between these two conditions is eventually understood, the interval that so often separates them should offer an opportunity of instituting preventive measures to forestall the rheumatic reaction.

From time to time small epidemics of acute rheumatism have been described, but acute rheumatism is not of itself regarded as infectious. It is the preceding sore throat which is the infectious element. Sore throats readily occur in epidemics, particularly when there is overcrowding, the agent spreading from case to case by droplet infection. Glover (1930) has shown that when such an epidemic visits a rheumatic community, the peak of the epidemic is likely to be followed in two or three weeks by a smaller peak of epidemic acute rheumatism. This may

be likened to an epidemic of diphtheria being followed by a much smaller epidemic of post-diphtheritic paralysis.

Of the specific fevers, those that are associated with sore throats are also liable to be complicated by acute rheumatism. Scarlet fever is the chief of these, but diphtheria, and less commonly measles and influenza, may also be followed by rheumatism. Occasionally infections elsewhere than the throat may be the starting-point. In one rheumatic child under the author's care an abscess at the root of a tooth, and in another broncho-pneumonia, were followed after the appropriate interval by a relapse of acute rheumatism.

Although not amounting to a definite disease, a state of prolonged debility is often a forerunner of acute rheumatism, so much so that the young debilitated child has been called the pre-rheumatic child. A poor diet, digestive disturbances, an unhealthy state of the lymph nodes in the body, and nervous overstrain are factors particularly likely to occur in the children of the poorer classes and lead to a lowered state of resistance against infections. It is not unreasonable to expect that the early and efficient treatment of symptoms of debility would diminish—among other infections—the incidence of acute rheumatism; indeed some indication of this is revealed in the sharp decline in the incidence of rheumatic fever that occurred between the years 1939 and 1942 of the war (Glover, 1943), coincident with a considerable rise in employment, an increased provision of milk and school meals for children, and evacuation *en masse* of school children from cities and towns into rural areas.

The infective factor.—It is now generally accepted that acute rheumatism is an infective process, although no one specific germ has as yet been accepted as the causal organism. One of the first organisms to be incriminated was a large bacillus isolated from the blood of rheumatic fever patients by Achalme in 1891, but later investigators were unable to confirm his findings. In 1900, Poynton and Paine isolated a small diplo-streptococcus—the diplococcus rheumaticus—from various lesions of acute rheumatism, and with this organism claimed to have reproduced in rabbits many of the manifestations of acute rheumatism. Although these claims have not received general acceptance, their investigations served to associate together streptococcal infection and acute rheumatism, an association which has become more and more widely accepted, until at the present day it is true to say that there is no serious rival to the streptococcal hypothesis of rheumatism.

The bacteriology of acute rheumatism is still complicated by the various results which have attended attempts to isolate organisms from either the blood or the local lesions. In addition to Poynton and Paine's organism, Small in 1927 obtained a non-hæmolytic non-methæmoglobin-forming streptococcus from the blood of rheumatic children. An anti-serum prepared against this organism—to which Small gave the name streptococcus cardio-arthritidis—was claimed to have beneficial results in the treatment of acute rheumatism. A year later Birkhaug described a non-methæmoglobin-forming streptococcus isolated from the blood and

local lesions of rheumatic children, with which he was able to reproduce in rabbits a non-suppurative arthritis and carditis. The difficulty of confirming these findings, and the growing number of different strains of streptococci which have been isolated have inclined others to the view that while acute rheumatism is closely connected with streptococcal infection, no one specific strain is responsible, but that rheumatism is one result of the conflict between the body and the streptococcal group of organisms.

Turning to the acute sore throats which so often precede an attack of acute rheumatism, investigations have shown that these are practically always due to infection by hæmolytic streptococci, the organisms falling into Lancefield's group A—*i.e.* pathogenic to man. Rheumatic children evidently react in a peculiar manner to streptococcal infection, for Todd (1932) has shown that the serum of these children contains a higher titre of anti-streptolysin than does the serum of non-rheumatic children ; and Coburn and Pauli (1939) have demonstrated that following hæmolytic streptococcal tonsillitis the rise in titre of this antibody is more slowly developed in rheumatic as compared with non-rheumatic children, but increases rapidly just before the appearance of rheumatic manifestations.

The present bacteriological position may be summed up in the following way. From time to time various non-hæmolytic streptococci have been isolated from rheumatic lesions, but there is no convincing evidence that any one of them is the specific cause of the disease. Meanwhile the importance of the acute sore throat which often precedes at a definite interval an attack of acute rheumatism has received renewed recognition. In general these sore throats are the outcome of hæmolytic streptococcal infection ; they may arise sporadically, or occur in epidemics spread by droplet infection.

Many difficult questions at once arise. Streptococcal throat infections among the child population are common enough, but acute rheumatism follows only in a small proportion. This is illustrated by the fact that non-suppurative arthritis occurs as a complication of scarlet fever (a known source of streptococcal infection) in under 5 per cent. of cases, and rheumatic carditis as a sequel is even less frequent. The conception of acute rheumatism as due to the invasion from the throat or elsewhere of living streptococci which settle in small foci in the heart and other tissues, and there provoke a rheumatic lesion, is difficult to correlate with the frequently negative findings on culture of rheumatic lesions and the general failure to demonstrate a streptococcal blood infection. The claims of Green (1939) and Collis (1939) to have recovered hæmolytic streptococci from post-mortem cultures of heart valves affected by rheumatism must await confirmation. The development of acute rheumatism after the initial throat infection appears rather to depend upon some altered condition of the individual, which enables products from the sore throat to set going an acute rheumatic reaction. In other words certain peculiarities of the soil may be necessary in order that the seed of rheumatism may flourish.

The allergic factor.—Within recent years an attempt has been made

to explain the phenomena of acute rheumatism by supposing them to be due to an allergic response of the tissues to streptococcal infection. Such an explanation entails preliminary changes in the tissues before rheumatic manifestations can appear, and incidentally marks an entirely fresh outlook on the pathogenesis of the disease. There are certainly good grounds for giving the allergic theory of rheumatism careful consideration.

Allergy is a term introduced by von Pirquet to signify an altered condition of the body cells, induced by contact with some foreign substance. Such substances are usually of a protein nature, and their effect is to render the cells hypersensitive to this particular substance. When the cells are in this hypersensitive state, further contact with the foreign substance gives rise to a violent reaction of which normal or non-sensitized cells are incapable. Bacterial allergy, which has been invoked to explain acute rheumatism, is a state of hypersensitivity of the body, or of certain cells of the body, induced by repeated contacts with the products of disintegration of bacteria. When an ordinary bacterial infection occurs, recovery is brought about by an attack against the invading organisms, which are killed and broken down. In this process, the products of bacterial lysis may enter the blood stream and produce a state of hypersensitivity in tissues far removed from the original site of infection. It is now known that bacteria are composed of two chief portions: a nucleoprotein fraction, and a carbohydrate fraction; it is probable that the nucleoprotein fraction is chiefly concerned in the production of hypersensitivity. Further, in a family of organisms such as the streptococci, which is composed of several strains, a part of the nucleoprotein is common to the whole family, so that a state of hypersensitivity induced by one strain might be roused into activity by a later infection with a different strain. Viewed in this light, the family of streptococci in general may as likely be responsible for acute rheumatism as any one particular strain.

Several investigations have been separately carried out to determine the hypersensitivity of rheumatic children to streptococcal products by means of intracutaneous tests. Before the possible relation between hæmolytic streptococcal infection and acute rheumatism had been suggested, Swift and others had shown that rheumatic children were more sensitive to injections of filtrates of non-hæmolytic streptococci than were control children. More recently the soluble products of fragmented hæmolytic streptococci have been used; this latter material was found to be more potent in producing skin reactions than that obtained from non-hæmolytic streptococci, and again rheumatic children were more sensitive than the control cases. Thus of 200 rheumatic children skin tested with hæmolytic streptococcal endotoxin, 71 per cent. gave positive reactions, compared with 23 per cent. of a similar number of non-rheumatic children (Green, 1942). Whereas these skin reactions may be taken to denote previous sensitizing infections with streptococci, they do not afford a specific test for rheumatism, since control cases may also react. Some significance should probably be attached to the fact that positive reactions only begin to appear in the child population at about the third

year of age, the incidence rising from then until puberty, after which no further increase is noted. The age incidence of these reactions resembles that of acute rheumatism.

There can be no doubt that mild streptococcal infections are common enough in early childhood for sensitization to take place. The throat, though not the only, is probably the most frequent focus of such infections, and the presence or absence of the tonsils appears to make but little difference. The living conditions that accompany poverty not only increase the likelihood of throat infections, but also retard recovery, and by prolonging the period of infection probably heighten the state of sensitivity or allergy. The child in this state is likely to exhibit not only a general state of debility, but such symptoms of the pre-rheumatic state as vague pains in the limbs and an irritable nervous system. Children of the well-to-do are also liable to streptococcal infections, but their surroundings are such that they can generally make a rapid and complete recovery, and if hypersensitivity develops, it will probably be short-lived. In this connection, it may be pointed out that positive skin tests in rheumatic children with the lytic products of hæmolytic streptococci tend to diminish after a period of six months from an attack of acute rheumatism. So long as the child is in this phase of hypersensitivity, the possibility of acute rheumatism is imminent; it needs but an acute streptococcal infection to fire off a train of symptoms which may include one or all of acute polyarthritis, carditis, subcutaneous nodules, or chorea.

The position has been well summarized by Coburn (1940), who considers that heredity and environment combine to produce persons who do not handle respiratory infections with hæmolytic streptococci in a normal manner. Their immune response is inadequate, with the result that the cells of the reticulo-endothelial system become sensitized. Subsequent contact of antigen and antibody within the sensitized cells gives rise to an abnormal reaction leading to the characteristic inflammation of rheumatic fever.

Virus theory.—The possibility that acute rheumatism might be associated with a virus infection has received attention, but investigations have proved disappointing. Virus-like bodies were obtained from pericardial and pleural exudates in rheumatic children (Schlesinger *et al.* 1935, and Eagles *et al.* 1937), and were found to be agglutinated by sera from resistant cases of acute rheumatism, but these results have not been confirmed, and Eagles and Bradley (1939) have since doubted whether these bodies should in fact be classed as viruses. The virus theory would seem to be on the wane.

Morbid anatomy and histology.—With the exception of the small sessile vegetations on the cardiac valves, the exudate in the pericardium, and the subcutaneous nodules, the principal morbid changes in acute rheumatism are of microscopic dimensions. The essential histological features consist of multiple small foci of inflammation situated for the most part in the connective tissues, particularly in and around small vascular branches. The distribution is widespread, and not merely confined to the heart and neighbourhood of joints. The type of tissue

response may be mostly proliferative or exudative, depending upon the site of the lesions ; exudation is seen when surface membranes are involved, such as the pericardium and the synovium of joints ; proliferation characterizes the connective tissue response, and is well exemplified by the Aschoff nodules in the heart.

Myocardium.—The Aschoff nodules of the connective tissue comprise the typical lesion. Although they only occur in rheumatic disease, they are not always to be found even when post-mortem examination shows death to have been due to rheumatic heart disease. They are found in close relation to the coronary arterioles—often in the adventitial coat—and are rounded or spindle-shaped structures varying in size from 0·1 to 0·5 mm. Each nodule consists of a small central necrotic area surrounded by a zone of œdema. Near the centre there occur large cells which are thought to be derived from the connective tissue, and are characteristically multinucleated. The nuclei are centrally arranged, giving the cell an appearance like the giant cells of Hodgkin's disease. There may be one or several of these cells. The periphery of the nodule is made up of a collection of plasma cells and lymphocytes, with an occasional eosinophil cell. The number of nodules varies considerably, but they are most likely to be found under the endocardium of the left ventricle near the insertion of the mitral valve. As a rule the conduction tissue of the heart is spared, which accounts for the relative infrequence of clinical evidences of abnormalities of rhythm. How long the Aschoff nodules remain as such is not known, but their ultimate destiny is to be replaced by scar tissue. In addition to the typical nodules a more diffused interstitial infiltration of the myocardium with lymphocytes is sometimes found.

Endocardium.—The changes in the endocardium are characteristic. Just below the free edges of the valves, on the side opposed to the blood stream, occurs a thin line of sessile, firmly attached yellow vegetations, each about as large as a pin's head. They occur most frequently on the mitral valves, then the aortic, tricuspid, and pulmonary in that order, and are often found on the chordæ tendineæ. The vegetations result from the necrosis of the valvular endothelium followed by a coagulable exudate from the valve tissue, together with the deposition of a minute platelet thrombus from the blood stream. Eventually the vegetations become cicatrized. It is now realized that the formation of vegetations is dependent upon interstitial inflammation within the valve, as was pointed out by Coombs and Swift, and that such valvulitis may indeed occur without the appearance of vegetations. The changes within the valve consist of swelling with infiltration of lymphocytes, plasma cells, and in some cases focal cellular accumulations resembling Aschoff nodules. The much greater importance that attaches to the inflammatory changes within the valves as compared with the formation of vegetations on the valve surfaces must be emphasized. It is doubtful whether such vegetations play any part in the production of physical signs, and they are seldom of prognostic significance. The contraction of the valves and chordæ that is found in old-standing cases of mitral disease is due to

cicatrization consequent upon the valvulitis, rather than to the actual vegetations. The demonstration by Bayne-Jones of a normal network of minute vessels in the valves, derived from the coronary arterioles and from the vasa vasorum of the aorta and pulmonary artery, has explained how the infection of acute rheumatism reaches the interior of the valves. The localization of the vegetations at the line of closure of the valve flaps is attributed to a locus minoris resistentiæ due to the repeated contacts of the valve flaps during closure, while the order of frequency of vegetations on the different valves coincides with the degree of vascularity of the valves combined with the amount of mechanical strain put upon them.

Changes in the endocardium of the left auricle, characteristic of rheumatic infection, have been described by MacCollum. The affected area is situated close to the posterior cusp of the mitral valve ; the surface of the endocardium becomes puckered and ridged, and later is thickened and scarred. In the sub-endocardium extensive cellular infiltration takes place with the formation of numerous Aschoff nodules, the large Aschoff cells being often forced into palisade-like columns by the elastic tissue.

Pericardium.—Rheumatic pericarditis is almost invariably accompanied by both myocardial and endocardial lesions. The changes may be limited to a small area, but as a rule the entire pericardium is involved. In the acute phase, the sub-pericardial tissues are swollen and show the same cellular response as does the myocardium, the Aschoff nodules being particularly well developed. The surface of the pericardium is hyperæmic, the lining membrane shows a patchy denudation, and is covered with a fibrinous exudate, which in severe cases may cause separation of the visceral and parietal layers by an inch of gelatinous-looking material. With a less extensive exudate, the pericardium shows the typical bread-and-butter appearance. Accumulation of free serous fluid to any gross extent is unusual, and this is of clinical importance should the question of tapping the pericardium arise. The great area of cardiac dullness which may be reached in acute rheumatic pericarditis is more often due to dilation of the heart muscle than to accumulation of fluid, so that tapping is seldom advisable.

Adhesions between the two pericardial layers soon form, and may be so diffuse that the ensuing organization completely obliterates the pericardial space. Exactly the same process may take place between the outer surface of the parietal pericardium and the adjacent pleura, mediastinum, and diaphragm. When organization of adhesions in these situations takes place, the heart becomes tethered to its surroundings, which leads to gross hypertrophy of the myocardium, and gives rise to the clinical picture of " adherent pericardium."

Blood-vessels.—The widespread nature of the pathological changes in acute rheumatism has been demonstrated by Pappenheimer and von Glahn, who have described focal cellular infiltrations of lymphocytes, polymorphonuclear leucocytes, and multinucleated giant cells in the coats of the aorta in relation to the vasa vasorum. The changes are purely histological. These authors have also described focal areas of necrosis, fibrinous exudate, and cellular infiltration in the blood vessels of the lungs,

kidney, perirenal fat, ovary, testis, and pancreas ; although typical Aschoff nodules were not found, the changes were regarded as being equally characteristic of acute rheumatism.

Lungs.—Apart from the occurrence of pulmonary congestion and occasionally pulmonary infarction during cardiac failure, changes in the lungs and pleuræ are not uncommon during acute rheumatic carditis. Pleurisy with fibrinous exudate is sometimes to be found, mostly over the left lower lobe, and the late development of pleuro-pericardial adhesions has already been mentioned. During the acute stage of carditis, it sometimes happens that an impaired percussion note and diminished air entry with perhaps tubular breathing are to be found over the lung bases, more often to the left side than the right. In some of these cases the lung is found at autopsy to be collapsed, but in other cases it is swollen, engorged, and consolidated. Naish and Fraser have both described the condition as an acute interstitial pneumonia characterized by cellular infiltration of the alveolar wall, proliferation and necrosis of alveolar cells, and the presence of multinucleated giant cells, the lesions resembling Aschoff nodules, and presenting a specific rheumatic picture.

Joints and connective tissues.—The exudate in the joints is turbid and albuminous but not purulent. Focal lesions comparable to the Aschoff nodules in the heart have been found in the synovia and joint capsules, and Shaw has described them in the connective tissue at the junction of muscle and tendon.

Subcutaneous nodules. –The subcutaneous nodules that may occur over bony prominences and along the course of tendons are characteristic of rheumatism, and are almost without exception accompanied by carditis. When cut across, they have a yellowish pink colour, becoming grey as they get older. The histological appearances are essentially similar to the Aschoff nodules—in the centre an area of necrosis and fibrin, surrounded by œdematous connective tissue containing large multinuclear cells, many lymphocytes, plasma cells and fibroblasts. According to Swift, the larger nodules represent an accumulation of submiliary nodules. That these submiliary nodules may occur more extensively than is usually recognized was suggested by Poynton and Still, who observed *post mortem* in the neighbourhood of subcutaneous nodules numerous more minute nodules not sufficiently large to raise the skin. Vincent Coates has also described submiliary nodules particularly in the region of the spine as of common occurence in rheumatic children.

Changes in the blood.—In addition to rapid anæmia during acute rheumatic disease of the heart, a mild leucocytosis with relative increase of lymphocytes also occurs. Payne and others have also shown that the rate of sedimentation of the red cells increases with the activity of the cardiac lesions. Although the fluctuations in the sedimentation rate are not diagnostic of any particular disease, they afford a numerical index of the progress—good or bad—which any particular case is making, and repeated estimations have proved very helpful in guiding treatment during the early convalescent stage.

PATHOLOGY OF CHOREA.—Chorea is so seldom fatal that opportunities

for studying the morbid changes seldom arise. Fatal cases are also generally complicated by rheumatic carditis, which may account to some extent for the vascular changes which have been described. The observed appearances have been diffuse, and less well defined than is the case with rheumatic lesions in other parts of the body. The principal findings have been congestion of the meninges, thrombosis of some of the smaller cortical vessels, a slight degree of small-celled infiltration in the brain substance, often in the neighbourhood of arterioles and particularly in the region of the basal ganglia, and also some degeneration of nerve cells. The changes are more noticeable in the hemispheres than in the mid-brain or brain-stem. These findings have been looked upon as indicating a meningo-encephalitis. "The absence of typical Aschoff bodies may well be due to the peculiar histological structure of the brain, and the vascular and perivascular lesions are strongly reminiscent of rheumatic lesions elsewhere in the body" (Sacks). The absence of any nervous sequelæ after chorea, with the possible exception of obesity in a few cases, makes it seem unlikely that any permanent scarring or destruction of cerebral tissue takes place. The cerebro-spinal fluid is unaltered with the exception that Warner has shown the calcium content to be reduced by as much as 15 per cent. The cause of the calcium deficiency is not clear. The anatomical localization for the movements of chorea is also uncertain; the striatal region, the corpus Luysii, and the neighbourhood of the red nucleus have all been held responsible; Wilson, from a detailed study of the movements in chorea, holds responsible an afferent disorder of the cerebello-thalamo-cortical mechanism, but points out that no single anatomical site for lesions underlying the development of chorea is to be expected. When chorea is uncomplicated by carditis, the sedimentation rate of the red cells remains unaffected throughout the course of the illness.

Clinical course of acute rheumatism

In many cases before symptoms of acute rheumatism appear, the child passes through a period of indefinite ailing and debility, sometimes with a history of repeated sore throats and often complaining of *aches and pains in the limbs*. Although the term subacute rheumatism has been applied to this state, it is not met with in all cases of frank rheumatism, nor is it necessarily followed by more serious rheumatic manifestations. Similar complaints in children may be found coupled with such diseases as asthma and tuberculosis. Other common causes of aching pains such as flat feet and simple muscular fatigue must also be borne in mind. So-called rheumatic pains are most common in the legs, but may also occur in the arms, neck, or round the chest; they can often be localized over the attachments of ligaments and muscles, but do not actually occur in the joints—at all events they do not restrict the joint movements. Often they are not related to fatigue, and are as likely to wake the child at night as to happen during the day. More striking is their frequent relation to damp weather.

The chief evidence for regarding these pains as rheumatic rests on their clinical association with other manifestations of rheumatism. In 52 out of 266 children with rheumatic heart disease, pains in the limbs over several months was the only evidence of rheumatism that preceded the discovery of the heart lesion. A history of limb pains preceded 15 out of 197 cases of chorea.

In the *treatment* of children suffering from "rheumatic" pains, general hygienic measures are of the first importance. It is significant that these children practically never complain of pains while they are away at a convalescent home. Damp draughty houses predispose to these pains, new houses being often as bad in this respect as old ones. The child should wear long stockings and thick boots, and in wet weather provision should be made for the child to change into dry shoes at school. Sleeping at night between blankets should be advised. Sodium salicylate, which is of great service in acute rheumatic arthritis, is often disappointing in dealing with these pains. The external application of liniment of methyl salicylate is more helpful; rubbing with the liniment for a few minutes will generally dispel the pains, which, however, are likely to return so long as the general health remains poor. To rectify this, a period of convalescence and the judicious use of a suitable tonic such as equal parts of syrup of ferrous iodide and malt extract are often of value.

Onset of acute rheumatism.—Acute rheumatism may begin in a variety of ways. The cases that definitely follow a sore throat usually exhibit either acute arthritis or acute carditis or both; in other cases chorea is the first manifestation, and in roughly a third of these there is also cardiac involvement. Fortunately for the patient, chorea and acute arthritis seem never to coexist. In a third group carditis is the only manifestation, and the onset may be so insidious that the heart affection is only discovered on routine examination. This was so in 14 per cent. of 266 cases of rheumatic heart disease under the author's care. Unfortunately the rheumatic process seems to be none the less destructive for being insidious in onset, in fact these cases tend to run a slowly progressive course towards mitral stenosis, a course which is difficult to influence by therapeutic measures.

Acute rheumatic arthritis.—The symptoms of rheumatic arthritis are often milder in childhood than in adults, and the classical description of warm, painful, red and swollen joints, one joint being affected after another, is seldom completely fulfilled. The affected joint is invariably warm and painful, but swelling is not always evident, while a red flush over the joint is less common than swelling. Occasionally only one joint is affected; when this happens to be the right hip, the association with fever and vague reference of the pain to the lower abdomen may simulate appendicitis. More commonly the knees, ankles and wrists are affected in sequence. The small joints of the hands and feet may also be implicated, and there may be also considerable wasting of the small muscles of the hand simulating acute rheumatoid arthritis. Tenosynovitis in the palm of the hand may also occur, and unless precautionery measures are taken, may lead to flexor contraction of the fingers. Spasm of the flexors

of the knee-joints may occur early, and cause acute flexion which if neglected may lead to much subsequent trouble. The temperature is raised as a rule to about 101° F., but hyperpyrexia is seldom encountered at the present day. The tongue displays a thick white fur, and the breath may be offensive. Heavy sour-smelling sweats affect adults rather than children. Clinical evidence of cardiac involvement is found in a large proportion of cases; of 133 instances of rheumatic arthritis at the rheumatism clinic at the Children's Hospital, Great Ormond Street, 70 per cent. showed evidence of heart affection. Coombs has stated that every child with rheumatic polyarthritis may be assumed to have an affected heart also, although clinical evidence of this may not always be found.

A feature of rheumatic infection, no matter what clinical form it takes, is the inability of the patient to establish a lasting immunity after one attack. Of the 133 cases previously mentioned, 21 experienced a second attack, and 2 had three attacks. The shortest interval between any two attacks in that particular series was six months.

Treatment.—The child should be nursed recumbent in bed between blankets, the bedclothes being raised off the joints by a cradle. Movement of the child must be gentle, and should be reduced to a minimum. The diet should be liquid, such as water, milk diluted with water, barley water, broths, or weak tea. The bowels are usually constipated, and calomel ½ grain is indicated at the onset. The joints should receive local treatment by being wrapped in a strip of flannel wrung out of methyl salicylate liniment, and then covered with cotton wool. Sodium salicylate is the most valuable drug for internal use, rapidly relieving the pain and incidentally reducing the temperature. It should be used for its former effect. To a child of seven years, 10 grains should be given every four hours, combining it with double the dose of sodium bicarbonate in order to prevent the onset of salicylate poisoning. This dose should be continued until the pain has been relieved, and then reduced to thrice daily. It is generally wise to continue this drug for a further three or four weeks, otherwise the fever and joint pains may return. Occasionally sodium salicylate is not well tolerated, and its place may be taken by acetylsalicylic acid with equally good results. The presence of cardiac involvement will of course determine how long the child must stay in bed; in the absence of physical signs of heart disease, the child should be put through a leisurely convalescence, getting up from bed after an interval of about six weeks from the onset.

Rheumatic carditis.—The onset of carditis is in rare cases fulminating, and within a few days the child is prostrate, pallid or livid, with rapidly increasing dilatation of the heart until death supervenes. A subacute onset is more usual. If the child is up and about, languor and loss of energy, shortness of breath, and præcordial pain are complained of, and on examination cardiac dilatation is found with loud bruits perhaps already present. When carditis supervenes while a child is under observation in bed—perhaps on account of arthritis—increasing pallor is noticed, the pulse rate and respiration rate rise, and unless the child is receiving salicylates, two or three degrees of fever are usual.

The earliest signs of carditis are those of myocardial dilatation, comprising a feeble apex beat outside the left nipple line, an increasing area of cardiac dullness, a short first sound at the apex with an increased pulmonary second sound, and persistent tachycardia. There may be a soft systolic bruit at the apex, but at this stage a bruit is the least important of the physical signs. With careful treatment in this stage, recovery is often complete.

In progressive cases, the sequence of changes may be rapid or gradual, depending on the severity of the injury to the heart. Increasing dilatation and a profound anæmia are ominous. The murmers at the apex develop in a definite order. At first there is a systolic bruit becoming conducted to the left axilla. This is followed by reduplication of the second sound at the apex, and then the second portion of the reduplicated sound slurs off into a mid-diastolic murmur. This is the most common murmur to be heard in diastole in childhood. The mid-diastolic bruit has its point of maximum intensity just internal to the apex beat, and is localized, often not covering an area greater than a crown piece. When the disease progresses further, the mid-diastolic murmur may be replaced by an early diastolic bruit, and this in turn is often interchangeable with a short presystolic bruit, the latter being heard when the heart is rapid, the early diastolic reappearing as the heart rate slows. The short presystolic bruit is temporary, unaccompanied by a thrill, and quite distinct from the long rumbling crescendo presystolic murmur of established mitral stenosis.

As the acute infection of the heart subsides, the murmurs just described will often be found to retrace their steps. After a few weeks the early diastolic and short presystolic murmurs settle down into a mid-diastolic bruit, which may then persist for several months or years. In some cases the mid-diastolic murmur and even the systolic murmur may disappear, and as far as one can tell the heart appears to be normal. On the other hand, mitral stenosis may slowly develop from the stage of systolic and diastolic bruits; in that case the first sound at the apex becomes louder and sharper, making the systolic bruit sound as though it begins with a puff—the so-called bellows bruit. Several years must elapse, however, before mitral stenosis is fully developed. Of the author's cases, the shortest period in which this occurred was three years, and often it takes double that time. Sometimes the systolic bruit at the apex becomes harsh or squeaky, indicative of a stiffening valve, with a correspondingly bad ultimate outlook.

Aortic regurgitation occurs in about 6 per cent. of rheumatic hearts; almost invariably the mitral valve is involved as well; the aortic lesion appears later than the mitral, and is often detected for the first time following a relapse of the cardiac infection. It is interesting to notice how often the combination of aortic with mitral regurgitation relieves the child of much of the breathlessness and discomfort that is attendant on a pure mitral lesion.

Although vegetations on the tricuspid valve are not uncommonly found in children dying of acute rheumatic carditis, symptoms during life of tricuspid disease are rare. Pulmonary valvulitis is only seen in the

post-mortem room, and that rarely. The diastolic bruit occasionally detected in the pulmonary area is of aortic origin. Disturbances of cardiac rhythm are relatively uncommon, although extra-systoles, degrees of heart-block, and auricular fibrillation may all occur. They are fully considered in chapter XXII.

Electrocardiogram.—The electrocardiographic changes consist of prolongation of the P-R interval, inversion of the T wave in leads I and II, and abnormalities of the S-T segment. These are not specific to rheumatism, but are indicative of an inflamed myocardium, and they are not invariably present. They may gradually disappear entirely, and therefore have little prognostic significance. With regard to the P–R interval, it must be remembered that this varies in health with the age of the child, becoming longer as childhood advances.

Pericarditis.—Occasionally rheumatic pericarditis occurs as a fleeting attack lasting only a week, and with few symptoms beyond slight fever and the presence of pericardial frictions. Much more frequently it is part of a severe acute carditis which may prove fatal. Often it occurs as a form of rheumatic relapse in a child who has already had previous attacks of heart disease. Although the classical sign of pericarditis is friction, evidence of a grave disturbance may be present some days before this sign appears. The temperature rises in two or three days to about 102° F., the pulse becomes rapid and weak, the respiration rate increases, and often the child vomits, or may be troubled by a frequent dry cough, or becomes restless. The face has an anxious expression, and pallor rapidly develops which is often accentuated by slight œdema of the face. Pain is variable, and is often made worse by movement; the movements of the diaphragm are diminished. At first the heart action is turbulent, and there may be a triple or canter rhythm at the apex. When friction appears it is first heard as a rule towards the base of the heart; it may occur as a to and fro superficial scratch or be systolic only; it may remain localized, but more usually becomes audible over the whole præcordia. The area of cardiac dullness may rapidly enlarge, so that the left border may extend into the left mid-axillary line. The heart sounds become soft, and evidence of cardiac failure such as œdema of the lungs, rapid swelling of the liver, and œdema of the feet, may appear. In cases such as these, the temperature may be persistently subnormal, and this should be regarded as of grave omen. During the acute stage an impaired percussion note and distant tubular breathing may be found at the bases of the lungs, particularly about the lower angle of the left scapula. As the violence of the attack subsides, the signs of cardiac failure may slowly regress, and recovery from the pericarditis may be complete. In other cases after some weeks of slight improvement the signs of failure reappear, and death slowly overtakes the child. When there has been associated pleurisy or mediastinitis, recovery from the acute illness is likely to be followed by the development of signs of adherent pericardium (p. 956).

Cardiac failure.—Apart from the failure which may occur during an acute attack of carditis, gradual failure resulting from the mechanical disability of scarred valves or from adhesion of the pericardium to sur-

rounding structures is more often met with in adolescence and early adult life than during childhood. Death in childhood from rheumatic carditis generally happens during or soon after an acute attack. The signs of cardiac failure are the same in childhood as in adults, and consist of cough and orthopnœa from pulmonary congestion, vomiting, distension of the liver, jaundice, ascites, œdema beginning in the extremities, and

FIG. 325—RHEUMATIC NODULES ON THE ELBOW.

albuminuria. Auricular fibrillation may also occur. The temperature is usually subnormal. Venous thrombosis, and gangrene of the fingers or toes, are rare complications. The youngest instance of ascites due to cardiac failure in the author's experience was a boy five years old, who had acquired severe mitral disease four years previously, but such a case is exceptional.

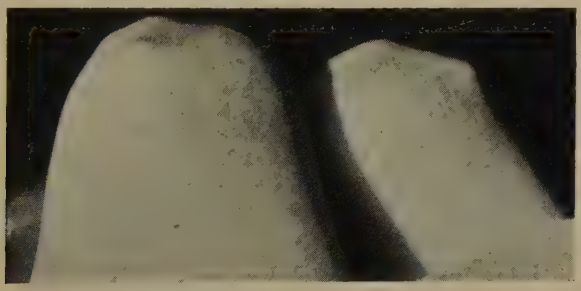

FIG. 326.—RHEUMATIC NODULES ON KNEES.

Death, either during the acute phase, or from gradual cardiac failure, is sometimes preceded for a few days by a changed mental state in which the child will have no one near him except perhaps one particular nurse, who must do everything for him; even the parents may be abruptly dismissed from the bedside; restlessness increases, and a most pitiful fear often grips the child, which is only relieved by opium or heroin.

Associated rheumatic phenomena.—SUBCUTANEOUS NODULES.—These nodules have attracted great attention, both on account of their

diagnostic importance and because they are so constantly associated with cardiac rheumatism. They are found most frequently over bony points; favourite sites are the elbows, patellæ, knuckles, styloid processes of the radius and ulna, the tendon of the palmaris longus, and the flexor tendons of the fingers. They may also be seen over the malleoli, the tendons of the tibialis anticus and peronei, and over the vertebral spines, the scapulæ, and iliac crests. Large nodules may be found over the occiput; usually as big as a large pin's head, over the occiput they may be massed into lumps the size of a hazel nut. In some cases the skin becomes reddened over them, but as a rule it is unaltered, and the nodule slips under the finger and is not tender. They are often multiple, come out in crops, and may vanish as mysteriously as they appear. In other cases they may last for months and even become covered by an adventitious bursa.

Erythema marginatum.—This is a characteristic eruption of rheumatism. It appears as numerous, slightly raised red streaks which are generally circular, covering an area about as large as a shilling, or they may coalesce, and then have an irregular wavy outline. The rash occurs principally on the trunk, both back and front, and may also appear on the limbs. It does not itch. It comes out quickly within a few hours, and may be evanescent, or may persist for several days with constantly changing shape. It is likely to recur, and in the author's experience it has always been associated with evidence of cardiac rheumatism. Of other skin rashes, purpura occasionally occurs, and may be severe. Here also may be mentioned epistaxis; it may occur once or repeatedly, and either during an acute attack of rheumatism, or between attacks. It is particularly likely to be met with in children who have aortic disease.

Diagnosis.—The early diagnosis of rheumatic heart disease may sometimes offer considerably difficulty when a child has a soft systolic bruit at the apex, and the heart is not enlarged. In many of these the bruit is only temporary, and disappears when the general health improves. A history of acute rheumatism or chorea would indicate that the bruit is organic. Organic systolic murmurs are often more easily heard when the child is lying down or lying on his left side. They also show little variation with the phases of respiration. The presence of a murmur at the apex during diastole is an unmistakable sign of organic disease.

The presence of tachycardia may also give rise to difficulty, because while it may be expected so long as the inflammation of the heart is active, it is also frequently exhibited by nervous children during examination. It is often difficult when a child is convalescing from an attack of rheumatic carditis, to determine the stage at which a tachycardia may safely be disregarded, and the patient allowed greater freedom of movement. Schlesinger has drawn attention to the value in such cases of taking the pulse rate while the child is asleep. In normal children the sleeping pulse is about 10 beats per minute slower than the waking pulse. In the presence of active carditis the sleeping pulse approximates to the waking pulse, and is also continuously above the normal; on the other hand a rapid waking pulse which is unaccompanied by a raised sleeping pulse points to a nervous tachycardia.

The differential diagnosis of acute rheumatism is not as a rule difficult. Both scurvy and syphilitic epiphysitis may be distinguished from rheumatic arthritis by the different age incidence and the presence or absence of supporting evidence of the former conditions. Other forms of arthritis—septic, pneumococcal, tuberculous—will be determined by the history, associated disease elsewhere, and the absence of other rheumatic manifestations. There is vital importance in distinguishing acute osteomyelitis ; the onset is more acute, the fever higher, the degree of toxæmia is much more severe, tenderness and pain are extreme, and the lesion is epiphyseal rather than articular. The immobility of the limb with rheumatic arthritis may simulate acute poliomyelitis, but actually slight movement of the rheumatic limb is possible, the tenderness is localized to the joints, and the reflexes are present. As regards the carditis, the points of differentiation from congenital morbus cordis, and infective endocarditis—which is rare in childhood—are dealt with in chapter XXII. In the severe anæmias of childhood, such as acute leukæmia and aplastic anæmia, the pronounced pallor and the presence of loud cardiac bruits with some dilatation of the heart may at first cause some difficulty in differential diagnosis from rheumatic heart infection, but the examination of the blood will reveal the true condition.

Prognosis.—The prolonged study of individual rheumatic children which is now carried out in the various special rheumatism clinics has taught that, at any rate in the milder cases, complete recovery from rheumatic carditis is possible. Figures taken from the rheumatism clinic at the Children's Hospital, Great Ormond Street, indicate that this result may be expected in about 10 per cent. of the children. Cases that begin under the age of five years are usually severe, and the prognosis, both immediate and remote, is bad. Although death during childhood may be the outcome of a first attack of carditis—this was so in 4·6 per cent. of 405 first attacks of rheumatic carditis recently analysed in South Australia—more usually it follows a relapse of rheumatic infection, and the mortality rate from rheumatic carditis steadily rises throughout the years of childhood.

The remote prognosis is difficult to foresee owing to inability as yet to control relapses, and because there is no means of telling whether an immunity has been established. A child may for example come under care for a mild attack of passing arthritis or chorea, and yet four years later be completely crippled by an attack of carditis. Relapses become less likely as the age of puberty is reached. Apart from the possibility of relapses, the presence of signs of adherent pericardium brings closer the day of cardiac failure, whilst the presence of a whistling systolic bruit at the apex, or a " bellows " murmur, indicates a progressively sclerosing type of lesion. A mid-diastolic bruit at the apex may eventually disappear after persisting for several months. Mitral endocarditis not of the progressive type is often compatible with a long and useful life. Although the breathlessness of mitral stenosis is often lessened by the advent of aortic disease, and life for the child may become more tolerable, the ultimate prognosis is affected adversely, for few of these patients survive

adolescence. The presence of nodules is usually an indication of severe and permanent damage to the heart; erythema marginatum is of less prognostic importance.

Prevention.—The treatment of rheumatic inflammation of the heart, both in its acute and chronic phases, is fully discussed in chapter XXII. The desirability of prevention is obvious in a disease which causes as much permanent disability as does rheumatic carditis, particularly as in spite of careful treatment a complete cure cannot as yet be reckoned upon.

A clinical study of rheumatic heart disease strongly points to throat infections as an ætiological factor, and not unnaturally this has led to a widespread movement in favour of tonsillectomy in the hope of diminishing the incidence of acute rheumatism. Whether or not this hope has been justified is dubious, but the balance of evidence is not in favour of the removal of tonsils simply as a prophylactic measure against rheumatic attack. Both first attacks and relapses of rheumatism seem to occur as readily in tonsillectomized as in non-tonsillectomized children; the only difference is that when the tonsils have been removed the acute tonsillitis is replaced by an acute pharyngitis. The present position may be put in this way, namely that the presence of rheumatism is not an indication for removing the tonsils; the question of tonsillectomy in rheumatic as in other children must be decided by the local condition of the tonsils, a history of repeated sore throats, and by evidence that they are interfering with the child's general health.

The interval of one to three weeks which so often elapses between the occurrence of an acute sore throat and acute rheumatism appears to offer an opportunity for prophylaxis, the sore throat acting as a warning of the possible advent of acute rheumatism. At the present time, two or three days after a sore throat has subsided the child returns to school and passes from medical care. Consequently the later development of carditis is likely to pass unnoticed until severe and permanent damage to the heart has taken place. The earlier a case of rheumatic carditis is diagnosed and cared for, the better is the chance of a complete cure, and much might probably be accomplished if the custom was widely adopted of keeping children under medical supervision for a month or so after a sore throat. Such supervision obviously must be arranged through the school medical service. Unfortunately many mild sore throats in children are overlooked because the child makes no complaint; experience shows that these mild infections are just as liable to be followed by rheumatism as are the more severe attacks.

In the case of children who have already had one attack of acute rheumatism, and who get an acute sore throat, the writer believes that some degree of prevention may be secured by the use of acetylsalicylic acid, as was first pointed out by Schlesinger. The drug should be given at the time of the sore throat and continued for four weeks, the dose for a child between five and eight years being $7\frac{1}{2}$ grains thrice daily, and 10 grains thrice daily for older children. During the course the child should be kept at rest. Not only is the likelihood of a rheumatic relapse thereby lessened, but should a relapse occur it will often be of a minor and abortive

character, consisting perhaps of fever for two or three days with mild joint pains, or a temporary dilatation of the heart, or even a fleeting pericarditis which subsides within a week.

It might be expected that penicillin would exert an effect in preventing hæmolytic streptococcal throat infections in a manner comparable with the sulphonamides, although daily injections extending over months would be an obvious drawback. There is however ample evidence that penicillin given by mouth when the stomach is empty can produce a systemic effect. Recently Pitt-Evans (1950) has shown that a daily oral dose of 100,000 units of penicillin lowers the carrier rate for hæmolytic streptococci in the throats of rheumatic children to one-sixth of the carrier rate in a control group of rheumatic children, and consequently the liability to rheumatic relapses is also lowered. Penicillin has an advantage over sulphonamides in being relatively non-toxic.

Mention must also be made of cortisone and adreno-corticotropic hormone (ACTH) in the treatment of acute rheumatic polyarthritis and early rheumatic heart disease, although it is as yet too soon to draw final conclusions. Reports indicate that the fever and joint swellings subside in a few days, and if that were all there would be no advantage over the effect of salicylates. Whilst, however, the influence of salicylates on rheumatic carditis is disappointing, there is evidence (Barnes and Smith, 1950) that cortisone and ACTH can rapidly dispel the early signs of cardiac involvement ; the heart rate returns to normal within a week or so, while at the same time the prolonged P-R interval in the electrocardiogram shortens to normal and the sedimentation rate of the red cells drops to a normal level within two to three weeks. Such results are encouraging, although it remains to be seen whether a more insidious rheumatic damage to the heart follows at a later date. Cortisone does not appear to influence rheumatic heart disease acquired in previous attacks of rheumatic fever.

The beneficial effect of the sulphonamide group of drugs on sore throats has led to their employment in rheumatism. It is generally agreed that they are without effect in the treatment of acute rheumatism, and even when given at the time of the sore throat they have not prevented rheumatic relapses (Coburn, 1939). They have, however, been given throughout the school year from October to June with the object of preventing sore throats, thereby forestalling rheumatic attacks, and the results have been favourable (Coburn, 1941 ; Thomas, 1941 ; Hansen, 1942). For the drug to act in this manner a blood sulphonamide level of 4 mgm. per c.cm. is sufficient, and the dose has been from 1 to 3 grammes daily. Of 352 rheumatic children treated in this way 6 experienced a rheumatic attack, while in an untreated control group of 356 rheumatic children 77 suffered a relapse of rheumatism. Such a method of prevention has its drawbacks—toxic symptoms appeared in about ten per cent. of the children ; when treatment was stopped, sore throats and rheumatic relapses proved capable of reappearance ; nor can it be held to be a practicable measure to submit all rheumatic children to such prolonged drug-taking.

The fact that acute rheumatism is so much more common among the

poorer population indicates that measures tending to improve the living conditions would equally tend to a reduction in the incidence of rheumatism. Good housing schemes for the avoidance of overcrowding and damp, and the cultivation of a higher level of general hygiene in such matters as clothing, cleanliness, fresh air, and diet, are steps in the right direction, but constitute ideals towards which a nation can move but slowly. Meanwhile the most hopeful aspect of prevention would appear to lie in the control and follow-up of acute infections of the throat, in which so much of acute rheumatism has its beginning.

CHOREA

Synonym.—Sydenham's Chorea : Rheumatic Chorea.

Chorea is a disorder of the nervous system characterized by involuntary spasmodic movements, irregularity and jerkiness of voluntary movements, and by emotional disturbances. The pathology of this condition has been described earlier in this chapter ; the remarks made concerning the ætiology of acute rheumatism equally apply to chorea. It may, however, be repeated that chorea preponderates in the female sex, roughly two girls being affected for every boy. In addition, the influence of nervous strain is often noticeable. Children who are mentally alert, intelligent, quick at school and eager for scholastic promotion are much more likely to be affected by chorea than are dull and placid children. Psychical influences other than worry over school work also seem at times to initiate an attack of chorea. In one child the fright of a thunderstorm was apparently sufficient to precipitate an attack ; street accidents increasingly appear as the alleged cause ; punishment at school is sometimes indicted as a cause, though it can be often shown that the punishment was given for behaviour which was really attributable to incipient chorea. In other words it is frequently difficult to decide where the line is to be drawn between a condition of nervous overstrain favouring chorea and a condition of nervous disturbance due to the presence of the disease.

Association with other rheumatic manifestations.—Chorea is so often associated with other forms of acute rheumatism that it is now widely regarded as the cerebral expression of rheumatic infection. Accepting this view, it must be pointed out that of all forms of acute rheumatism chorea is the one most likely to occur alone without other rheumatic accompaniments. Of the writer's 197 cases of chorea, rheumatic carditis occurred in 52, acute polyarthritis preceded five cases, and in fifteen instances pains in the limbs either accompanied or followed the chorea. Thus it will be seen that roughly a third of the children with chorea had also other forms of rheumatism. The most frequently associated rheumatic condition is carditis, and if the heart is affected in a choreic child, this is most likely to take place at the time of the first attack of chorea. Like all rheumatic conditions, chorea is likely to relapse, but if the heart escapes in the first attack of chorea, it is more likely to remain unaffected in later attacks.

Symptoms.—The onset is occasionally acute, and then follows some definite nervous shock or fright, but a gradual onset is much more usual. In the early stages, the child is noticed to drop things out of her hands, becoming fidgety, and emotional, making grimaces or showing mental dullness and a failure to concentrate the attention. When the child is examined, the expression is often heavy and dull, with the mouth drooping open, but the movements are the most noticeable feature. They vary considerably in severity, and are characteristically haphazard and do not show repetition of any one particular movement. At one moment the mouth is twisted or the eyebrows raised, a moment later a shoulder is shrugged, the hand jerked, or the feet shuffled. It is impossible to foretell what muscle group will next be jerked into activity. Clucking noises with the tongue are frequent, and sighing often occurs due to inco-ordination of respiratory movements. The speech is affected, becoming hesitating and the words clipped short or explosively uttered. Rapid alterations from laughter to tears and vice versa are common. In a milder case the movements may be brought out by watching the child undress herself, the frantic efforts to undo buttons and hooks leaving no doubt of the child's complaint. When asked to show the tongue, the movement is ill controlled, and the tongue may be withdrawn very sharply or returned with a slow deliberation. When asked to stretch out the hands, the wrists are flexed and the fingers hyperextended while the thumb makes repeated dipping movements. The tendon reflexes are variable; the knee jerks may be diminished or lost, or the contraction of the quadriceps may be prolonged so that the leg remains extended for a second or two, or the muscle may contract rapidly two or three times until the leg is fully extended.

Certain special manifestations of chorea need mention. The movements may be much more marked on one side of the body, but a true hemi-chorea is doubtful. The movements cease during sleep, but when the movements are violent it is difficult for the child to get to sleep, and there is then a real danger of exhaustion. Speech may be so much affected that it is lost altogether, and for a month or two the child may be completely aphonic. Such loss of speech is, however, never permanent, but recovers as the choreic movements subside. Occasionally the mental change may develop into acute mania, the child behaving in an odd way, tearing up the bedding, soiling herself, shouting and abusing all and sundry. Eventually the mentality recovers, but it may take six months or longer before the child's behaviour settles down to normal. Then lastly there is limp or paralytic chorea. This is the most severe form, and in the author's experience is always accompanied by severe cardiac rheumatism. The child lies limply in bed unable to raise a limb; the muscles are toneless, and when the arms or legs are raised from the bed and released, they flop back helplessly just like a limb affected with poliomyelitis. The tendon reflexes are all lost. The choreic movements are almost entirely abolished, but if a careful watch is made small purposeless movements at the wrist, fingers and ankles, or an occasional twitch of the face are seen, and reveal the underlying condition.

The condition of the heart is of great importance. In 250 cases of chorea observed by Still, cardiac bruits were recorded in 155. A systolic murmur at the apex is the most common, and is often accompanied by some evidence of cardiac dilatation. In about a quarter of these, the evidence of cardiac involvement disappears during convalescence, and it might be thought in such cases that the bruit was a functional one. It is known, however, that rheumatic carditis is capable of recovery, and if chorea is accepted as a rheumatic manifestation it is certainly wiser to treat a systolic bruit during chorea with all the respect that rheumatic carditis deserves. In other cases the presence of a diastolic as well as a systolic bruit, the appearance of subcutaneous nodules, or the development of pericarditis leaves no doubt of the presence of heart disease. On the other hand, there may be nothing to indicate infection of the heart, and then the heart rate is often noticeably slow and deliberate, the pulse dropping to about 60 beats per minute.

Course and prognosis.—The course of an attack of chorea is long, and often exceeds the period of six weeks regarded as the average duration of the attack. In many cases the affection is observed in hospital to increase gradually in severity and then die down. Chorea of itself is rarely fatal. When death does occur, the child is completely exhausted by the violence of the movements. Nutrition fails, and unhealthy sores develop from the minor injuries which eventually arise from the continual damage to the skin by constant friction. A considerable number of cases may be severe enough to give rise to great anxiety, but when well nursed recovery is the rule. The complication of carditis is formidable, and affects the prognosis adversely; in fact much of the seriousness of chorea lies in the fact that it marks the child as a rheumatic subject who is liable to other and more fatal forms of rheumatism.

The severity of the movements is not a good guide to the duration of an individual attack; often the most troublesome cases to clear up are those in which the movements have never been anything but mild, and in some cases slight jerkiness of voluntary movements may persist for several months. Like all rheumatic conditions, chorea is prone to relapse. Of the author's cases fully a quarter experienced one or more relapses, whilst two children had as many as six attacks.

Diagnosis.—Although chorea in childhood is almost always rheumatic, typical choreic movements occasionally arise with other organic diseases of the brain. Encephalitis lethargica may be accompanied by choreic movements as may a cerebral tumour, and a typical display of chorea rarely arises during the last days of tuberculous meningitis. Choreic movements may also occur in children with congenital diplegia. These other causes of chorea are, however, all rare, and are associated with such signs of organic cerebral disease as enable the proper diagnosis to be made.

The most common condition with which chorea is confused is habit spasm. Typically a habit spasm consists of the frequent repetition of one movement, for example the child may repeatedly blink his eyes or pull his mouth to one side, and after a few weeks may change to some

other movement. The multiplicity of the movements in chorea enables the differential diagnosis to be made. Even in those cases of habit spasm in which the movements are numerous and complicated, there is an order about them which is quite foreign to chorea. On the other hand, mild cases of chorea sometimes drift on for months, and the choreic movements seem to become habitual. Such cases should be treated on the lines laid down for habit spasm.

Treatment.—It must always be remembered that the treatment of chorea is essentially the treatment of a case of rheumatism. It follows that before attempting any heroic measures for the chorea, the question if they are likely to be of service to the rheumatic state in general must be considered. The tender age and nervous temperament of these cases must also be constantly remembered, and it is wise to bear in mind that the great majority will recover, however simple the treatment. The first essential is adequate rest in bed, and to secure this the child should be nursed flat with one pillow. It will not do for the child to rest merely so many hours each day, the rest of the day being spent up and about. Skilled nursing is necessary, since for the first two or three weeks everything must be done for the child, and she should not even be allowed to feed herself. The room should be as quiet as possible, and in a hospital a quiet corner bed should be chosen. The old practice of screening off the bed is no longer held necessary, the quiet routine of ward life being more helpful to the choreic child. Great attention is needed to prevent abrasions of the skin, particularly in protracted cases when considerable wasting results; and the failure in nutrition leads to sores which are liable to become septic. When the movements are violent, it may be necessary to pad the cot.

When, as often happens, the child becomes particularly restless at night-time, and sleep is difficult to obtain, a warm sponging is often the most effective sedative, or a hot wet pack is a valuable means of soothing the child. Feeding may offer much difficulty; ample food is indicated, but much patience and skill may be needed to get the child to take sufficient nourishment. Thickened milk feeds, broths, and eggs are all valuable foods. The bowels are usually constipated, but require only simple purgatives.

Drugs.—There is no specific drug remedy for chorea, nor has it ever been shown that any drug used in chorea is able to prevent that most important complication of all—carditis. Bearing in mind that chorea tends to recover simply with rest, the dosage of drugs should never be pushed to dangerous limits. Sedatives are indicated when the movements are severe, in order to prevent the child from becoming exhausted. Chloral, chlorbutol, the bromides and phenazone are the most useful, their object being to give a reasonable degree of restfulness. A working rule for chloral is a grain a year for the first five years, but in the grave cases larger doses may be required, and for a child of seven years as much as 10 grains three times a day may be needed. When large doses are employed, the nurse must be warned to be on the watch for coldness of the hands and feet, feebleness of the pulse, and undue drowsiness. Chlorbutol is also a

drug that requires careful supervision, because it is to some extent cumulative. From 3 to 5 grains may be given three or four times a day. For milder cases phenazone in 5-grain doses with or without an equal amount of bromide may help the child to settle off at night. For maniacal cases, hyoscine hydrobromide $\frac{1}{500}$ grain or morphine may be necessary. Some years ago trial was made of a drug called "nirvanol," belonging to the barbitone group of hypnotics. The drug was given for a week or ten days, after which toxic symptoms of fever, a morbilliform rash, and eosinophilia were expected. Although when these symptoms appeared the choreic movements generally ceased, the drug did not prevent later attacks of chorea, nor did it prevent other rheumatic manifestations, and as its use is not without danger, producing in some cases prolonged mental confusion, it may be said to afford an example of how chorea should not be treated.

Another drug which has enjoyed popularity in the treatment of chorea is arsenic. It has been recommended in the acute stage of chorea, and in doses large enough to arouse toxic symptoms; but if it has any value at all it is chiefly in the period of convalescence, when it has sometimes seemed to hasten the return of the child to normal. For this purpose, 2 or 3 minims of Fowler's solution is an adequate dose. Sodium salicylate and acetylsalicylic acid, in view of their value in relieving acute articular rheumatism, have been given an extended trial in chorea, but it cannot be said that they lessen materially the duration of an attack.

Convalescence.—The time will come when the child should be allowed to begin to do things for himself and to sit up in bed; this will be when the movements have subsided, and when the child is no longer agitated by trying to perform some simple action. This stage is generally reached after three or four weeks, and then simple exercises to encourage co-ordinated movement, such as making a jig-saw puzzle or drawing with crayons, are useful. In the absence of cardiac involvement the child can generally be allowed up out of bed in about six to eight weeks, provided that the movements have completely disappeared.

When the child has recovered sufficiently to return home, it is often difficult to decide when a return to school should be allowed. At the rheumatism clinic at the Children's Hospital, Great Ormond Street, the average time that children with chorea have been away from school has been six months. This has seemed unnecessarily long in some cases, while others have relapsed on returning to school after an absence of twelve months. The home circumstances will largely influence the decision. If absence from school implies that the child will spend most of the day in the street, it is better for an early return to school to be made. When there is a garden, and the mother or some other responsible person is at home all day, six months away from school should be a minimum. A stay at a convalescent home for three to six months is valuable, particularly if a mild amount of education can be combined with the convalescence. In many cases half-day attendance at school for a term before allowing whole-day attendance has proved useful. Once a choreic child returns to school he soon makes up the ground he has lost through absence.

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CHAPTER XXIV

BLOOD DISORDERS

SIR LIONEL WHITBY AND G. H. NEWNS

INTRODUCTION

Alterations in a normal blood picture, whatever the age period, present to the physician and hæmatologist the difficulty of distinguishing primary disease of the hæmopoietic system from the reaction of the same system to some other disease. Extension of knowledge has greatly reduced the number of " primary anæmias," and it is now well recognized that most abnormal hæmatological findings are more an indication of disturbance of function than an exact diagnostic picture. Most blood changes are caused either by a nutritional deficiency or by some exciting or depressing disease ; they should be regarded as symptomatic blood disorders rather than blood diseases. A hæmopoietic reaction is dependent on many factors. Not the least of these is the individual, in whom general condition, nourishment, environment, development and heredity all have an influence. In childhood and infancy the assessment of the individual factor, from the clinical standpoint, is of first importance, if a proper interpretation is to be made of alterations in a blood picture. The hæmopoietic system of the child is extremely sensitive to extraneous influences. The younger the child the more the sensitivity. Alterations in the blood picture may therefore be no less dramatic and striking than the surprising clinical features which sometimes accompany such alterations. In an adult the hæmopoietic system has become stabilized to provide blood for a life uncomplicated by the factor of growth ; various tissues have served their purpose and have atrophied ; others have assumed a position far less important than in the growing child whilst immunity, acquired during the growth period, has reached a relatively stable state. In a child, the growth factor is extremely variable from one child to another and may be complicated by diseases rarely present in an adult. In a child, small errors in a diet have a more profound influence than in adult life. In a child, the lymphatic system is prominent and quickly reacts to extraneous influences so that it may be impossible to assess the significance of splenic, hepatic or glandular enlargement from a clinical examination alone. It is comforting to know that great enlargement of these organs, even when associated with a grossly abnormal hæmatological picture, has not always the same grave significance as in an adult. The causes of the so-called *von Jaksch's syndrome*—a severe anæmia associated with primitive leucocytes and enlargement of the spleen, liver and lymph glands—are multiple and complex, whilst the syndrome itself may indicate a disease inevitably fatal within a short period, a disease which may subside as rapidly and spontaneously as it appeared, or a disease associated with a long period of chronic invalidism. From this brief introduction, it should be clear that

the hæmatologist can rarely provide an exact diagnosis. This will have to be made from a correlation of the hæmatology with the clinical features, which the physician will in turn orient with his experience of these findings in relation to age, growth, development and the other permutations and combinations which go to make pædiatrics such a fascinating study. A correct interpretation of hæmatological findings demands a knowledge of the anatomy of the hæmopoietic system and of the normal standards of reference for the various age periods.

THE HÆMOPOIETIC SYSTEM IN INFANCY AND CHILDHOOD

Blood formation in the embryo begins in the area vasculosa of the yolk sac at an early stage, and is followed by cell formation from the body stalk and placental site. Later, the liver, spleen and thymus become actively hæmopoietic and, finally, the bone marrow. There are three successive phases. These are known as the *mesoblastic phase* occupying the first two months of embryonic life; the *hepatic phase* which includes splenic and thymic blood production and which is most active from the second to the fifth month, and the myeloid phase, which begins during the fifth month. Gilmour (1941), from studies on an 18 mm. embryo, found the liver parenchyma to be one of the earliest and most active sites for leucopoiesis. Until about the middle of fœtal life, however, comparatively few leucocytes are produced ; at this time the bone marrow is developed and begins to function as a blood-forming organ. Soon after birth, the marrow is normally the only place where red cells and granular leucocytes are formed, although the liver of both premature and full-time infants may contain active intralobular blood islands at birth and sometimes up to the fifteenth day of life (Gilmour, 1941). After great blood loss or in severe anæmias, and especially in infants, the liver, spleen and the pelvis of the kidney may again assume blood-forming activity.

At birth and for the first three or four years of life all the bones in the body contain red hæmopoietic marrow. About the *age of seven* the marrow in the shafts of the long bones becomes less active. At this age the marrow is pale red, in that it contains an appreciable amount of fat.

At the *age of ten to fourteen* a patch of yellow fatty marrow appears at the distal end of the shafts of the long bones and this gradually extends proximally, becoming complete distally until, at the *age of twenty*, the entire red marrow in the long bones has been replaced by yellow marrow with the exception of the upper ends of the femur and humerus. The change from red to yellow occurs in the carpus before the bones of the forearm and leg, and again, in the forearm and leg before the humerus and femur. The changes are illustrated in fig. 327.

The fibula, radius and ulna follow a similar course to the tibia, whilst the humerus resembles the femur and the os innominatum the vertebræ. It will be appreciated that the marrow cavities of an infant are completely filled with active hæmopoietic tissue and, in contrast with what occurs in an adult, there is no reserve space for expansion which can fill with active

marrow in times of need. It is for this reason that under conditions of anæmic stress an infant develops accessory hæmopoietic centres in the liver, spleen, kidney and sometimes even the muscular tissue ; in older children such centres have usually atrophied and are incapable of reactivation. The lack of reserve marrow space is also one of the reasons why hæmorrhage in infancy is so badly borne.

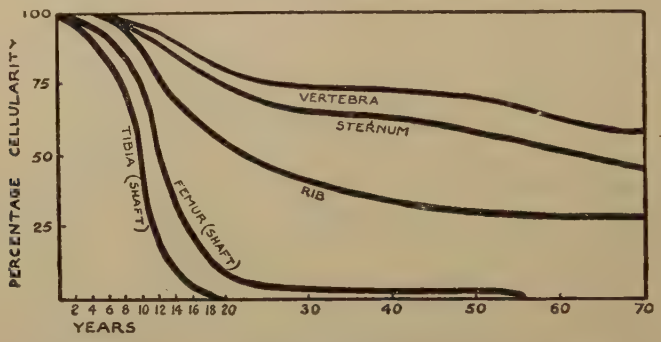

Fig. 327. The Proportion of Cellular Red Marrow in Different Bones at Different Ages.

(All the illustrations in this chapter are from *Disorders of the Blood*, by L. E. H. Whitby and C. J. C. Britton, by permission of J. & A. Churchill Ltd.)

Bone marrow

Under normal conditions red cell production is essentially normoblastic, so that the marrow contains, as nucleated cells in the erythrocytic series, none other than *normoblasts* in various stages of maturation, and, their precursors, the *proerythroblast* and the undifferentiated *hæmocytoblast*. Hyperplasia of the marrow as a reaction in response to such simple stimuli as hæmorrhage, hæmolysis or iron deficiency is fundamentally normoblastic—an exaggeration of the normal process. Megaloblastic hyperplasia, an abnormal reaction, is rarely seen in infancy and childhood, but may occasionally be found with certain alimentary conditions. In megaloblastic hyperplasia the process of red cell formation becomes diverted from the proerythroblast onwards, so that a series of *megaloblasts* is formed, in lieu of normoblasts, which mature as *macrocytes* or *megalocytes*. This type of erythropoiesis is found in the embryo, but otherwise is most characteristic of the dyshæmopoiesis of adult pernicious anæmia. This terminology and mode of development of red cells is that generally accepted by modern hæmatologists. The term *erythroblast* is used as a comprehensive word to include all nucleated red cells whether of the normoblast or megaloblast series.

The marrow in infants and children, when compared with that of an adult, shows a larger total number of all types of nucleated red cells as well as a higher proportion of lymphocytes. During the first two years of life the total nucleated cell count may be as high as 700,000 per c.mm., with a high proportion of lymphocytes ; the mature polymorphonuclear count

is lower than in older children (Diwany, 1940). In childhood, the total nucleated cell count has a range from 75,000 to 150,000 per c.mm.; the myeloid cells are less than in an adult, so that the myeloid-nucleated red cell ratio varies from three to one to one to two. This is mainly due to the relatively small numbers of fully mature segmented polymorphonuclears, which rarely exceed 10 per cent. The lymphocyte percentage varies from 20 to 30. Vogel and Basson (1939) have made extensive studies of the marrow in childhood, whilst Diwany (1940) reviews the literature of sternal puncture.

PHYSIOLOGICAL CHANGES IN THE BLOOD DURING INFANCY AND CHILDHOOD

The interpretation of hæmatological facts in a child requires a knowledge of the average findings in healthy children at different ages; these differ considerably from the ordinary adult criteria.

Hæmoglobin.—The extensive investigations of Mackay (1931; 1933b) have produced authoritative figures for the hæmoglobin content of infants from within twenty-four hours of birth and, at monthly intervals, up to the end of the first year of life. Fig. 328 shows the proposed standard hæmoglobin curve for the first year of life, which Mackay constructed from investigations on breast-fed and artificially-fed London children; on this has been superposed the calculated ideal normal curve. The results of Elvehjem *et al.* (1937) derived from 1,350 normal infants agree approximately with Mackay's ideal curve. On the other hand, certain American authorities give the high values of 23·9 grammes per 100 c.cm. (165–170 per cent. Haldane) for the amount of hæmoglobin at birth.

From fig. 328 it will be seen that during the first three months of life there is a sharp drop in hæmoglobin from the high birth figure to, approximately, 75 per cent. of normal at the age of three months. The fall is even greater in premature infants in whom the three-month figure may be less than 50 per cent. Treatment with iron does not correct the physiological decrease in hæmoglobin during the first three months of life. From the age of three months to six months there should be a gradual rise in hæmoglobin from 80 to 90 per cent. of normal and the figure should then remain steady for the remainder of the first year. After the first year, the taking of a mixed diet, richer in iron than maternal milk, or artificial food should cause the hæmoglobin to reach 90 to 100 per cent. of normal or 13 to 14·8 gramme per cent., save perhaps for minor fluctuations at puberty. In artificially-fed infants, during the first year, the hæmoglobin is 1 to 4 per cent. lower than in those who are breast-fed (Mackay 1933c); Hutchison (1938) found a difference of as much as 9 per cent. The mean corpuscular hæmoglobin concentration at various age periods is shown in the table on p. 1047.

With infants it should be borne in mind that the technique and the site from which the blood is obtained make appreciable differences in the hæmoglobin reading. Mackay's curve was constructed, using Haldane's method, on samples taken from a prick in the heel with a triangular cutting

needle, the foot being warmed before the prick was made. If the acid hæmatin method of Sahli be used for infants, the time allowed for conversion of the hæmoglobin should be a full sixty minutes in contrast with the thirty or forty minutes required for adults ; this is because of the presence of fœtal hæmoglobin which differs chemically and spectroscopically from that of other children.

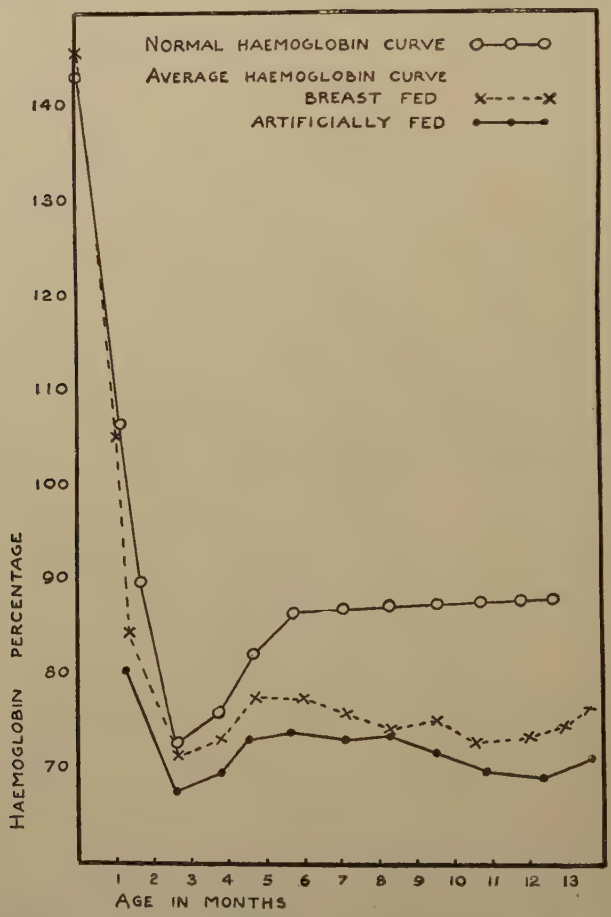

FIG. 328.—THE NORMAL HÆMOGLOBIN LEVEL DURING THE FIRST YEAR OF LIFE. (Mackay).

Note : 100 per cent in the diagram = 13·8 gm. per cent. and not the more usual figure of 14·8 gm. per cent. Percentages should therefore be read approximately 5 per cent. lower.

Red cells.—The red cell count at birth is from $6\frac{1}{2}$ million to $7\frac{1}{4}$ million per c.mm. ; the high figures of $7\frac{1}{2}$ to 8 million which are often quoted are but rarely found. There is usually a slight rise in the cell content of capillary blood a few hours after birth, due, probably, to circulatory adjustments following on birth ; after the first few hours there is a steady decline to 5 to $5\frac{1}{2}$ million per c.mm. at the end of twelve days (fig. 329).

During infancy the red cell count of the artificially-fed child is slightly lower than that of breast-fed infants. The following table shows the hæmatological standards for various age-groups setting out both the average and the normal range :

TABLE 48

Age Period	Number of Cases	Authority	Hæmoglobin (gm. per cent.)	Red cell (millions)	M.C.V. cu. microns	M.C.H.C. $\gamma\gamma$
1 to 10 days	195	Chuinard *et al.* (1941)	16·3 (12·3–20·3)	4·6 (3·4–5·8)	95·2 (74–116)	37
4 to 13 years	112 boys 103 girls	Osgood and Baker (1935)	12 (10–14)	5·0 (4·2–5·8)	72 (62–82)	32–34
12 to 17 years	100 boys	Goldhamer and Fritzell (1933)	11·55 (9·8–13·58)	4·7 (3·28–5·87)	—	—

M.C.V.—Mean corpuscular volume. M.C.H.C.—Mean corpuscular hæmoglobin concentration.

Immature cells.—The peripheral blood at birth usually contains a fair number of nucleated red cells, the normal number being 600 to 1,000 per million erythrocytes (Goldbloom and Gottlieb, 1929). On the other

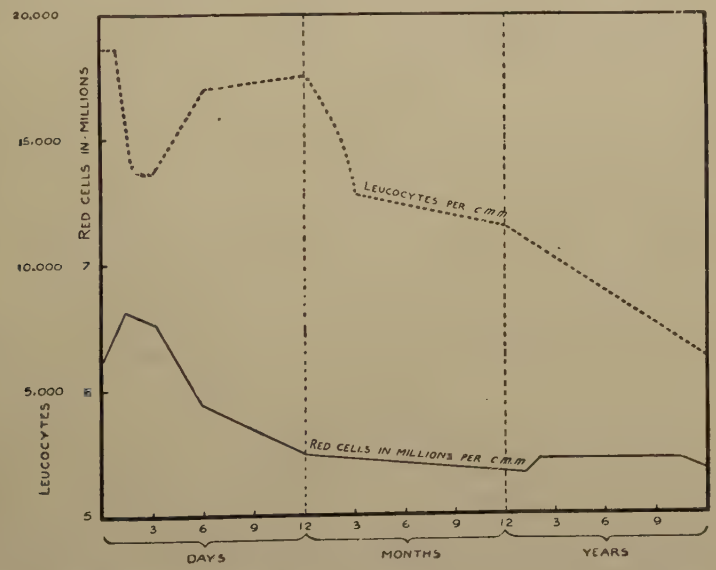

Fig. 329.—Red Cell and Leucocyte Counts from Birth to Twelve Years of Age.

hand, nucleated red cells are sometimes completely absent. The number usually falls to 20 to 50 per million red cells at the end of a week. The usual cells are late normoblasts, but in premature infants, earlier forms may be found, whilst nucleated cells are usually more plentiful. Reticulocytes

to the extent of 5 to 10 per cent. are present at birth, but fall to the normal adult figure of less than 1 per cent., during the first days of life.

Cell size and shape.—There is considerable anisocytosis at birth as well as a high average diameter. Van Creveld (1932) records a mean diameter of 8·41 μ in a full-term child fourteen hours old. During the first few weeks of life there are considerable changes in red cell size and distribution in both full-term and premature infants. During the first week of life the red cell distribution curve shows macrocytosis with much anisocytosis ; in the second week the macrocytosis increases. Thereafter the mean diameter for the premature child decreases more rapidly than in the case of the full-term infant, and, at the same time, anisocytosis becomes more marked. Van Creveld (1932) found that the mean diameter gradually fell to adult level in about a year or eighteen months. Parallel changes occur in the mean corpuscular volume. Anisocytosis becomes less in the full-term infant from the sixth week onwards and in the premature child after the tenth week.

The fact that an infant's red cells are larger than those of an adult has been responsible for the description of some infantile anæmias as macrocytic. It should be borne in mind that generalized macrocytosis may be brought about by acidosis whilst the reverse effect occurs with alkalosis. The mean corpuscular volume at various age-periods is shown in table 48.

Leucocytes.—The total leucocytes fall rapidly from about 18,000 per c.mm. at birth to about 14,000 two days later. There is then a rise, at first fairly sharp and then more slowly, to about 17,000 at twelve days ; from then onwards during the next twelve years the count slowly falls to the average adult figure of 6,000 per c.mm. (fig. 329). These approximate figures have a wide normal range and show considerable fluctuations (Kato, 1935) ; they are usually lower in premature infants. The method of feeding has little influence on the total leucocyte count, but it has an effect on the differential count (p. 1049). Consideration of the absolute numbers of polymorphonuclears and lymphocytes is more instructive than following the somewhat complicated variations which occur in the relative numbers of the two cells.

Fig. 330 shows that the polymorphonuclear leucocytosis present at birth declines in the first week of life to about 4,500 cells per c.mm. and that for the remainder of infancy and childhood the number of circulating polymorphonuclears is approximately the same as that of an adult. Lymphocytes, on the other hand, rapidly increase after birth, reaching a maximum at about the twelfth day ; they then decline slowly and reach the normal adult level at about twelve years of age. It is useful to remember that at four years of age there are approximately 4,000 per c.mm. of both lymphocytes and polymorphonuclears, and that the percentage of each is about 40.

The percentage figures for polymorphonuclears and lymphocytes show two main phases of complementary decrease and increase. The first phase is during the first twelve days of life, when the polymorphonuclears decline from 60 per cent. to 25 per cent., and the lymphocytes increase from 15 per cent. to 55 per cent. The second phase is a long one, from twelve days

to twelve years ; the polymorphonuclears slowly increase from 25 per cent. to the normal adult level of 60 per cent. and the lymphocytes decrease from 55 per cent. to 25 to 30 per cent. The point at which both are equal is about four years of age.

The more artificial the method of feeding during the first year, the more is the natural lymphocytic decline hastened. The lymphocyte of infancy is predominantly the large lymphocyte and the predominance gradually changes during childhood, until, at twelve years of age, the majority of cells are of the small type characteristic of an adult.

Eosinophils and basophils do not show any great variation from the

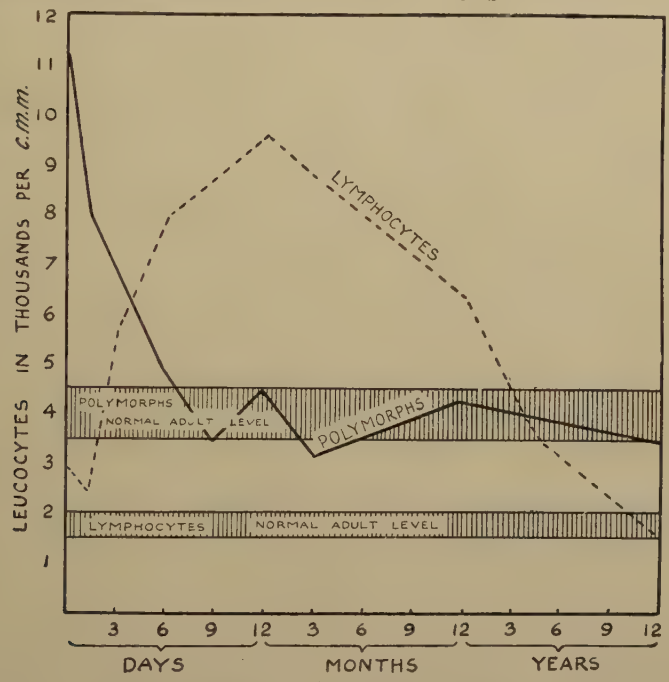

FIG. 330.—ABSOLUTE NUMBERS OF POLYMORPHONUCLEARS AND LYMPHOCYTES FROM BIRTH TO TWELVE YEARS OF AGE.

normal adult figures of 1 to 4 per cent. and 0 to 1 per cent. respectively. Premature infants often have an eosinophilia.

The monocyte is somewhat more abundant in the infant and child than in the normal adult—the average figure being 9 per cent. There is a definite monocytosis in the neonatal period lasting for about two weeks (Kato, 1935).

Primitive leucocytes are found in the circulation during the first few days of life, but it is unusual to find myelocytes or myeloblasts after the end of the first week. At birth myelocytes are commonly present to the extent of 2 or 3 per cent. and myeloblasts up to 1 per cent ; these primitive cells are more numerous in premature infants. Young polymorphonuclears, the so-called metamyelocytes, are found during the first fourteen days of life, but are normally absent at the end of the first month.

Coagulation factors.—Blood platelets are present at birth and from then onwards in the same numbers as they are found in adult blood, namely, 250,000 to 500,000 per c.mm. During the first few days of life the *coagulation time* is considerably longer than that found at a later period. This is due to the low plasma prothrombin which is normal for an infant; the birth level is 60 to 70 per cent. of the normal adult figure, but then falls to 20 per cent. or less in forty-eight hours, returning to birth level in about five days. The reason for the fall in prothrombin is that milk contains very little vitamin K (from which prothrombin is synthesized by the liver) and it is not until bacterial activity in the intestine becomes sufficiently established to affect synthesis of vitamin K from ingested milk that the prothrombin level can again rise to normal. Beveridge (1928) using the capillary tube coagulation time method of Wright found the following increases in infantile coagulation time, as compared with adults.

TABLE 49

Days of life	1	2	3	4	5	6	7	8	9	10
Percentage increase in coagulation time, as compared with adult.	22	43	41	38	27	18	23	11	8	6

These changes may also be convincingly demonstrated by the micro-method of Innes and Davidson (1941) for determining prothrombin time. The *bleeding time* by Duke's method is the normal adult time of two to five minutes (Beveridge, 1928). *Clot retraction* is normal.

Fragility of the red cells.—The blood of new-born infants shows minor degrees of hæmolysis in slightly more concentrated salines than in adults, whilst hæmolysis in dilute solutions may be less complete (Whitby and Hynes, 1935). Otherwise, the fragility test in infancy and childhood gives the same result as in normal adults.

Bilirubinæmia.—The icterus index which is high (7 to 10 units) at birth, rises to a peak in three to five days and remains high for the first twelve days of life. Jaundice is not apparent until the index reaches 15. The erythrocyte count at birth does not influence the development of physiological jaundice (Martin and Evans, 1935).

Iso-agglutinins.—Infants are born with their blood groups determined, but the only factor which is fully developed is the corpuscular agglutinogen. Natural iso-agglutinins are usually undeveloped, but may be present in low titre. But the blood of a new-born infant contains agglutinins passively acquired from the maternal circulation. With certain matings, this may give rise to the condition of erythroblastosis fœtalis (p. 1067).

Excluding pathological incompatibilities the blood of a mother is compatible with that of her new-born child for about the first week of life. After this time the passively acquired maternal agglutinins decline in titre and the child's own agglutinins gradually appear; they are fully developed within the first year of life.

Blood volume.—In normal infants the blood volume calculated in

relation to body-weight, is 50 per cent. greater than in adults ; it declines to 10 per cent. by the end of the first year. The total blood volume of an average 7 lb. infant at birth is about 300 c.cm. The volume doubles during the first year of life and gradually increases to about 2,500 c.cm. at puberty ; thereafter the increase is more rapid in males than females and is influenced more by physique than age (Brines *et al.*, 1941).

Disturbance of the water regulating mechanism of the body is a relatively common occurrence in early childhood. It should be borne in mind that hydræmia may give rise to hæmatological results which bear no relation to the true state of affairs unless interpreted in relation to total blood volume.

THE COLLECTION OF SPECIMENS

Methods, precautions.—In infants and children the collection of proper specimens presents peculiar difficulties, partly because of the small size of the patient's vein and partly because complete co-operation is not always obtainable. A number of micro-methods for various procedures have therefore been devised which require the minimum of blood for their performance. The following methods of collection may be practised :

(1) Complete blood examination.—A pathologist is in a far better position to make a competent report if he has an ample sample of blood in an isotonic anticoagulant with which he can fill his own pipettes and proceed to determine such factors as reticulocyte count, corpuscular volume, sedimentation rate, or platelet count, should his preliminary investigations indicate that such are required. The best samples are, therefore, supplied in tubes, preferably accompanied by two or three thin blood films made at the time of collection. The ideal sample is 2·5 c.cm. of blood collected from a vein into a tube containing the correct amount of Wintrobe's dry oxalate mixture, corked with a waxed cork and well shaken. The tubes are prepared by measuring into each tube 0·1 c.cm. of a solution containing 2 per cent. potassium oxalate and 3 per cent. ammonium oxalate and evaporating to dryness in an incubator. A battery of tubes can be prepared for the collection of smaller amounts (*e.g.* 0·05 c.cm. oxalate solution for 1·25 c.cm. of blood) obtained either by venepuncture or by free flowing capillary puncture, as the case may be. The prime essentials are exact amounts of blood and anticoagulant. The specimen should be sent to the laboratory with the minimum of delay. On such samples the following are the maximum times which may elapse between taking the sample and performing the test, if an accurate result is to be obtained. The times are shorter in hot weather. Twenty-four hours : hæmoglobin, red cell and leucocyte counts, blood platelets, reticulocyte count. Three to four hours : icterus index, van den Bergh reaction, fragility of the red cells, sedimentation rate, corpuscular volume, peroxidase test. Alternatively, a small tube containing 3 drops of 1 per cent. heparin, can be used to collect blood from a free-flowing puncture. The tube must be rotated during the process of collection. Heparin causes clumping of leucocytes, and specimens collected in this manner are unsuitable for leucocyte counts.

An easy method for performing a simple blood count is to supply the operator with two small bottles with glass stoppers containing, respectively, a small amount of distilled water or N/10 HCl and exactly 2 c.cm. of one of the diluting fluids for red cells. Into these bottles the operator places exactly 20 c.mm. of blood obtained from a needle prick with the pipette ordinarily used for an hæmoglobin estimation.

The hæmoglobin is estimated from one bottle and the red cells and

leucocytes from the other. Two or three thin blood films should also be supplied. The operator requires to be precise in his measurements and must take care that the outside of the pipette is wiped clean before discharging its contents into a bottle.

(2) Sedimentation rate.—Whenever a sample sufficiently large for an ordinary test can be obtained, this should be done, in that micro-methods, though informative, are not entirely satisfactory. For Wintrobe's method a 2·5 c.cm. sample of blood, as described in the preceding paragraph, is required. For Westergren's method the requirements are 1·6 c.cm. of blood collected into 0·4 c.cm. of 3·8 per cent. sodium citrate solution in a syringe. When no vein is available, the blood for Westergren's method may be collected into a test tube from a free-flowing puncture wound by the following technique : a test tube is marked at a level of 1·25 c.cm. ; into this tube place 0·25 c.cm. of 3·8 per cent. sodium citrate solution. The hand or foot is placed in a warm bath and then dried.

A suitable site is punctured and the blood allowed to drop straight into the citrate, being mixed by gentle shaking until the level of the mixture reaches the 1·25 c.cm. mark. This will provide enough blood for a 200 mm. column. Proportionate dilutions may be used for less quantities of blood, in which case a full Westergren's tube cannot be filled, but a reasonable correction can be applied for a column not less than 50 mm. long. Other micro-methods using special apparatus are those of Smith (1936) which requires no more than 0·3 c.cm. of blood, and the apparatus known as the Crista micro-sedimentometer supplied by Hawksley.

(3) Coagulation time.—The capillary tube method of Wright is most suitable for children. With this method, it is essential to have a freely flowing puncture wound and to perform a normal control at the same time.

(4) Prothrombin time.—The micro-method of Innes and Davidson (1941) is suitable for young subjects. Reference should be made to the original paper for the exact technique which enables the test to be made with the amount of blood required to fill a leucocyte pipette.

(5) Fragility of the red cells.—Simmel's method, as modified by Whitby and Hynes (1935) allows of an accurate quantitative fragility test on capillary blood, using red cell pipettes to collect the specimens.

(6) Bone-marrow.—In the new-born babe or infant the tibia, inferior and medial to the anterior tuberosity, is preferable to the sternum for the obtaining of samples or for the infusion of fluids. The sample should consist of exactly 0·25 c.cm. of marrow fluid added to a tube containing the evaporated residue of 0·1 c.cm. of a solution containing 0·2 per cent. potassium oxalate and 0·3 per cent. ammonium oxalate (Wintrobe's oxalate mixture, p. 1051). Smears should be made from the oxalated fluid within half an hour of collection. Material for section may be obtained by placing the sample in a wide centrifuge tube, which is then spun and the supernatant fluid gently removed with a pipette. To the deposit add 10 c.cm. of F.A.M. mixture (90 c.cm. of 5 per cent. mercuric chloride in absolute alcohol to which, at the time of use, has been added 10 c.cm. of 40 per cent. formaldehyde). Fixation occurs in twelve to twenty-four hours and sections of this material give an accurate picture of the architecture and cellularity of the marrow. This procedure avoids the necessity for trephine samples. In older children, puncture through the iliac crest gives equally good results.

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CLASSIFICATION OF ANÆMIAS

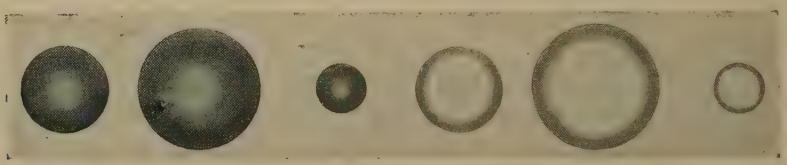
Anæmia may be defined as a state in which the quantity or the quality of the red cells is reduced below the normal level. The minimal requirement for maintaining a normal blood level is the provision of fully hæmoglobinized corpuscles sufficient to replace those cells that become effete. Anæmia must therefore occur when the production of cells is poor in quantity or quality and when blood loss or blood destruction outstrips the available supply of new cells. These fundamental facts form a basis for a classification of anæmia according to cause and provide the four main groups into which anæmias may be divided, namely:

(1) Dyshæmopoietic anæmias: due to inefficient blood production.
(2) Hæmolytic anæmias: due to excessive intravascular blood destruction.
(3) Hæmorrhagic anæmias: due to extravascular blood loss.
(4) Primary aplastic anæmias: due to primary disease of the erythron.

It is well known that primary disease of the erythron is extremely rare, but it is also recognized that the system is a delicate one and one which will only function in an orderly and efficient manner if supplied with an adequate amount of essential hæmopoietic substances. One large group of anæmias arises from malnutrition of the erythron, owing to a deficiency of essential blood-building materials. The recognition of a nutritional deficiency supplies a key to the treatment of many anæmias. Dyshæmopoiesis may be due to definite deficiencies of iron, liver principle, vitamins or internal secretions, and such conditions are readily amenable to simple specific treatment. On the other hand, problems of malnutrition involve not only intake but also a proper working of the processes of digestion and absorption. Alimentary factors, therefore, play a large part in the production of the dyshæmopoietic anæmias, and when this is the case, mere hæmatinic treatment, however specific, may achieve no more than a partial response. In addition, there is a large group of anæmias of which the mechanism is little understood but which are probably dyshæmopoietic owing to the

disorganizing action of such conditions as infection, nephritis, leukæmia or other diseases with which anæmia is constantly associated. These, in general, show very little response to symptomatic treatment with hæmatinics. Orientation of an anæmia into one of the four classes described above immediately emphasizes the symptomatic nature of the manifestation and gives an indication of the correct line of treatment. This, in principle, has two main objects: first, the elimination of the primary cause whenever possible, and, secondly, the prescription of the correct hæmatinic in order to hasten repair.

The anæmias may also be classified on a hæmatological basis according to variations in cell number, size, shape and hæmoglobin concentration. Elaborate clinical studies have shown that certain hæmatological types of anæmia are commonly associated with certain diseases. In practice, it is relatively rare for a blood examination to provide a specific diagnosis, but it can nevertheless often give a valuable pointer to the correct diagnosis, whilst an exact hæmatological analysis can indicate clearly what form of therapy should be employed for the anæmia *per se*. Wintrobe (1934)



Size:	Normal	Increased	Reduced	Normal	Increased	Reduced
Hæmoglobin concentration:	Normal	Normal	Normal	Reduced	Reduced	Reduced
Designation:	Normocytic Normochromic	Macrocytic Normochromic	Microcytic Normochromic	Normocytic Hypochromic	Macrocytic Hypochromic	Microcytic Hypochromic

FIG. 331.—DIAGRAMMATIC REPRESENTATION OF RED CELL SIZE AND HÆMOGLOBIN CONCENTRATION.

suggested the following four hæmatological groups based upon determinations of mean corpuscular volume and mean corpuscular hæmoglobin concentration: (1) macrocytic; (2) normocytic; (3) simple microcytic; (4) hypochromic microcytic. This simple classification is far more informative than a classification by means of the colour index because the index, being dependent upon two variables, cell size and hæmoglobin concentration, may sometimes be extremely misleading; it is possible for alteration in the two factors to be antagonistic and so cancel out the effect of both. Wintrobe's classification includes the anæmias commonly found in practice, but other types also occur as shown in fig. 331.

Whenever the mean corpuscular volume is greater than 94 cμ an anæmia is macrocytic; if between 78 and 94 cμ the anæmia is normocytic; if less than 78 cμ then microcytic. Whenever the mean corpuscular hæmoglobin concentration is less than 32 per cent., the anæmia is hypochromic. With certain exceptions, a macrocytic anæmia may be expected to respond well to liver therapy and hypochromic anæmia to treatment with iron; combinations of the two occur. Normocytic and simple microcytic anæmias rarely respond to treatment with these two hæmatinics.

DYSHÆMOPOIETIC ANÆMIAS OF INFANCY AND CHILDHOOD

Nutritional anæmia of infancy

Definition.—Hypochromic or hypochromic microcytic anæmia occurring in infancy as the result, almost always, of an inadequate intake of iron.

Ætiology.—Simple iron-deficiency in infancy may be due to deficient ante-natal storage of iron, to deficient post-natal supply or to a combination of both factors (Parsons and Hawksley, 1933). During gestation the fœtus acquires from the mother a store of iron sufficient to tide it over the time when the diet is deficient in iron, namely the milk-feeding period. Bunge (1892) showed that the iron content of young mammals is highest at birth, that it progressively diminishes during the milk-feeding period; that it does not increase again until the animal takes mixed food, and, that weight for weight, there is five times more iron in the liver of the new-born than in the liver of adult animals. Two-thirds of the iron present in the fœtus at birth is laid down in the last three months of intra-uterine life (Hugounenq, 1899). The store acquired from the mother is augmented by the iron derived from the hæmolysis of unwanted corpuscles during the first few weeks of life. As a general rule the fœtus gathers iron for its own purposes even from an anæmic mother. But this rule is not regarded as absolute by some authorities.

Hawksley and Neale (1933), for example, claim that there is a congenital type of nutritional anæmia, curable by supplying missing dietetic factors; they describe a number of cases of this type, but admit that before accepting an anæmia in a new-born child as of congenital origin, it is essential to exclude abnormal hæmolysis.

These workers consider that this congenital type of nutritional anæmia is due to a deficiency in the maternal diet; they differ from Baar and Stransky (1932) and other writers, who maintain that anæmia of the mother does not produce anæmia in the new-born child.

General experience indicates that although congenital nutritional anæmia may occasionally occur, it is a very rare condition, although the infants of anæmic mothers may develop the classical nutritional anæmia of infancy more rapidly or more severely than those born of normal mothers.

With these principles in mind, it will be clear that anæmia may readily occur if there is not a sufficiency of maternal iron available, as with the *anæmia of twin births*, if the fœtus has not had opportunity to lay down a full store of iron, as with the *anæmia of prematurity* (p. 1058), if the nursing mother is unable to obtain an ample diet and so give regular feeds of milk containing the full content of iron, as with the common *nutritional anæmia of infancy*, or, if the feeds be otherwise deficient in iron, as with some artificial foods and with *goat's milk anæmia*. At the end of the milk feeding period, the rapidly growing infant requires a diet richer in iron than maternal milk; *excessive prolongation of the milk feeding period* is inevitably associated with anæmia. Whilst the lack of iron is the fundamental cause of such anæmias, there are frequently additional factors

such as general undernutrition, alimentary disturbances, infection, toxæmia or wasting diseases which aggravate and add to the morbidity.

Age-incidence.—True iron-deficiency anæmia probably does not occur before the age of three months. This is Mackay's view (1931). She maintains that there is no evidence that nutritional anæmia is ever present at birth. As a rule the earliest age at which iron-deficiency anæmia makes its appearance is four months. Usually it develops after the sixth month, tending to appear rather later in the breast- than the bottle-fed infant. The lower the birth-weight the earlier the appearance of anæmia. In twins also anæmia tends to occur at an earlier age (see p. 1055). If the infant is not given a mixed diet at about six months but is kept on milk and cereals, the anæmia will progress and by one year of age may be quite severe. Milk feeding prolonged into the second year may result in very severe degrees of anæmia. For instance, our experience includes a child aged two years with a hæmoglobin of 4 gm. per cent. (28 per cent. Haldane).

Clinical features.—Nutritional anæmia is of insidious onset, so much so that babies often are severely anæmic, with a waxen colour of the face and extremities, before they are brought to the doctor. Often it is an intercurrent infection rather than the anæmia itself which leads the parents to seek medical advice. The anæmic infant does not, as a rule, look ill, unless a severe infection is present; it tends to be overweight and flabby. Activity is generally reduced and anorexia is a striking feature. In the later stages dyspnœa may be present and the heart may become dilated, and hæmic murmurs appear. Gastro-intestinal disturbances are common in these anæmic children. In the absence of infection, the spleen is not usually enlarged. Lymphatic gland enlargement does not occur.

The most serious feature of nutritional anæmia is the increased liability to infections. In Mackay's series (1931) the morbidity rate was twice as high in the anæmic group as it was in the control series treated with iron. The anæmic babies showed a greater liability to colds, otorrhœa, enteritis and bronchitis, which tended to clear up less rapidly than in the non-anæmic babies. These infections aggravate the anæmia and thus a vicious circle is established, which can only be broken by giving iron and so curing the anæmia.

Course.—Mild cases of nutritional anæmia may recover spontaneously if a mixed diet rich in iron-containing foods, such as vegetables or eggs, is given. There is a slow rise in the hæmoglobin level. Severe cases cannot be cured by diet alone and must be given adequate iron therapy.

Diagnosis.—The clinical recognition of anæmia except in severe cases is difficult; in the mild ones it is impossible. Infants with skin pallor are often diagnosed as being anæmic. Those kept indoors without fresh air or sunshine become pale and flabby and may simulate nutritional anæmia. The colour of the skin depends on many factors such as external temperature or the presence of pyrexia, and these may mask an anæmia. The colour of the lips, gums, ear lobes and palms of hands is a good indication of the presence of anæmia, although significant changes are only

present in the severer forms. In view of the frequency of nutritional anæmia a routine examination of the blood after six months is therefore desirable.

Hæmatology.—The anæmia is always hypochromic with a low mean corpuscular hæmoglobin concentration and colour index; it is frequently microcytic, although the high mean corpuscular diameter of infancy (p. 1048) may obscure this feature. Poikilocytosis is not usually prominent. Nucleated red cells, mainly late normoblasts, may be present in fair numbers. The bone-marrow shows intense normoblastic hyperplasia.

Treatment.—(1) Prophylactic.

Mother.—Whether or not by treating the anæmic mother it is possible to prevent anæmia in her infant is not proven. Yet it is desirable on general principles to eliminate any anæmia in the mother.

Infant.—Mackay maintains that all infants should be given iron as a prophylactic measure. Her investigations among infants in the East End of London, the work of Davidson and Fullerton (1937) in Scotland and Colver (1938) in London show that there is a high incidence of nutritional anæmia, mostly of the milder type, in infants in the poorer parts of the large cities. This anæmia can be prevented by administering iron. Mackay advises adding iron to the diet from the end of the first month. It can be given as an iron preparation, or incorporated in the milk. "Hemolac" (Cow & Gate) has been fortified with iron and ammonium citrate, 31½ grains to each pound of dried milk powder. An infant consuming 1 pound of milk powder in the week receives 4½ grains of the iron salt daily.

Alternatively the iron may be given in medicinal form, using ferrous sulphate or iron and ammonium citrate in a dosage of 5 grains a day. It is important to give small amounts of iron at first, otherwise colic and diarrhœa are likely to occur. Similarly, if "Hemolac" is used, it should be introduced gradually into the diet.

Many pædiatricians do not give iron to babies as a routine unless they be premature or twins; these last should unquestionably receive iron medication from the age of one month as they have a marked tendency to develop nutritional anæmia.

Early introduction of iron-containing foods into the diet, at the sixth month, will prevent much nutritional anæmia and render iron medication in the first year of life in a full-term infant unnecessary.

(2) **Curative.**—Iron must be given in bigger doses than those employed in prophylaxis. It must be introduced gradually otherwise gastro-intestinal symptoms may occur. The usual iron preparations given to infants are reduced iron, ferrous sulphate, and iron and ammonium citrate.[1] Ferrous salts appear to be more effectively absorbed and utilised than ferric salts. Reduced iron is converted by the hydrochloric acid of the gastric juice into ferrous chloride. In sickly infants suffering from infections, there is often hypoacidity of the gastric juice. It is desirable, therefore, to

[1] 1 gramme reduced iron ≡ 4 grammes of ferrous sulphate ≡ 3 grammes of exsiccated ferrous sulphate ≡ 4 grammes of iron and ammonium citrate (approximate equivalents).

administer hydrochloric acid in combination with reduced iron. Ferrous salts have the disadvantage that in solution they readily take up oxygen and become converted into ferric salts. Hypophosphorous acid and dextrose prevents this oxidation.

Mackay's prescription is :

Ferrous sulphate . . .	1½ grains.
Dilute hypophosphorous acid .	¼ minim.
Dextrose	20 grains.
Chloroform water to . .	60 minims.

This is a relatively stable mixture. Dosage of 5 grains upwards is necessary depending on the degree of anæmia.

About four to five days after iron therapy is started the reticulocytes begin to increase in number ; the reticulocytosis may reach a level of 10 to 15 per cent., if the dosage is adequate ; it gradually subsides in about ten days after the peak is reached. At the time of the reticulocytosis the erythrocytes rise fairly rapidly to normal levels. The rise in hæmoglobin is more gradual. There is also a general improvement in the clinical condition of the infant and any infection from which he is suffering usually begins to improve.

The rate of response to iron therapy varies greatly and there has been much speculation concerning the reason. The presence of a severe intercurrent infection may delay the response. The regenerative power of the marrow may also vary from patient to patient. Another possible cause is the use of iron salts of low solubility. It is important, of course, in addition to iron medication, to take specific measures against the infection.

The place of copper in the treatment of nutritional anæmia of infancy is still a debatable matter. Copper has been shown to be essential for the cure of nutritional anæmia in young rats, but there is no proof that the same holds good for the human infant. Mackay (1933) carried out a series of experiments in which two series of cases of nutritional anæmia were taken, one being given copper and iron, the other copper-free iron only. She came to the conclusion that copper deficiency played no part in the cases she was treating. It must be remembered that therapeutic preparations of iron salts contain minute amounts of copper, sufficient in most cases to supply all that is required. Parsons and Hawksley (1933), however, recommend a daily dose of 1 c.cm. of a 0·5 per cent. solution of copper sulphate per kilogramme of body-weight.

Blood transfusion has little place in the treatment of nutritional anæmia, but when it is severe it seems reasonable to give a blood transfusion as recovery is thereby greatly hastened and prolonged iron medication obviated.

Anæmia of prematurity

Infants born prematurely develop an anæmia in the first three months of life. The degree of the anæmia is roughly proportional to the degree of immaturity of the fœtus, which is roughly in proportion to the birth-weight. At birth the erythrocyte and hæmoglobin level in a premature infant are higher than in the full-term infant. In the ten days following birth there is a very considerable fall in the number of erythrocytes and in the

hæmoglobin, and the ultimate level reached is much lower than in a full-term infant. The erythrocytes and hæmoglobin continue falling until the eighth to twelfth week at which time the lowest level is reached. Subsequently the hæmoglobin and erythrocytes rise spontaneously to normal values by the seventh to eighth month. The hæmoglobin may, however, lag behind the erythrocytes. Nutritional disturbances, an inadequate diet or any congenital anomalies interfering with development may cause prolongation of the anæmia.

Iron does not cure the anæmia of prematurity which cannot therefore be due to an iron deficiency. Premature infants often develop iron-deficiency anæmia after the fourth to fifth month due to a combination of a deficiency of iron in the diet and a subnormal iron store in the liver at birth, which becomes rapidly exhausted.

Ætiology.—The cause of the anæmia of prematurity is obscure and various theories have been propounded. One view is that it is due to a deficiency in the iron storage of the liver, but this cannot be the cause of the initial drop in hæmoglobin, though it is probably the chief factor in the production of nutritional anæmia in later infancy.

Some think the anæmia is caused by a deficient production of blood by the hæmopoietic tissues of the premature infant, but Van Creveld and Heybroeck (1932) maintain that it is brought about by excessive hæmolysis and regard this anæmia as being of the hæmolytic type.

The excessive fall of the erythrocytes and hæmoglobin after birth in the premature infant if probably an exaggeration of what occurs in the full-term infant. The relative anoxæmia *in utero* demands a larger number of red blood cells and a higher concentration of hæmoglobin. After birth, since the lungs are a much more efficient respirator than the placenta, the excess cells are not needed and are hæmolysed. This hæmolysis, however, tends to be greater than it need be and an anæmia results. This theory of increased hæmolysis is supported by the fact that in full-term babies the icterus index falls to normal at the end of the second week, whereas in prematures it takes much longer to do so. In premature infants the physiological jaundice is more intense and more prolonged than in full-term infants.

Deficient blood production may also be another factor preventing recovery from the anæmia. The premature infant also grows extremely rapidly and its demands on the hæmopoietic tissue may outstrip the ability of the bone-marrow to provide the necessary red cells and hæmoglobin.

Symptoms.—The only clinical sign is pallor. There is no impairment of appetite or physical activity. The spleen may be enlarged, probably due to increased hæmolytic activity.

Hæmatology.—The anæmia is normocytic. Reticulocytes are relatively scarce. After the twelfth week the erythrocytes steadily increase but the hæmoglobin rises more slowly and hypochromic cells with a tendency to microcytosis appear.

Treatment.—Iron therapy has no effect on the anæmia. After the third month when the hæmoglobin is beginning to rise administration of

iron hastens recovery. The infant has a poor store of iron and finds it difficult to repair the hæmoglobin deficiency. Moreover, the administration of iron at this period prevents the development of nutritional anæmia which is so liable to occur in the premature infant.

Van Creveld and Heybroeck (1932) found that a combination of vitamin D and liver or of reduced iron and vitamin D, prevented the development of severe grades of anæmia. Blackfan, Baty and Diamond (1930) recommend repeated blood transfusions to prevent severe anæmia.

Nutritional anæmias of late infancy and childhood

Definition.—A group of anæmias with complex hæmatological features arising from failure to ingest, absorb, eliminate or utilize essential hæmopoietic substances.

Ætiology.—Iron deficiency is the commonest cause which may arise as a prolongation of the nutritional anæmia of infancy when the child has not been efficiently treated or when economic conditions do not permit a proper mixed diet. Anæmia is common with acute and chronic intestinal infections and in all forms of chronic diarrhœa or other states when absorption is deficient as with tuberculous adenitis or cœliac disease. Malnutrition, toxæmia, infection and hypochlorhydria may contribute to a vicious circle. It will be obvious that alimentary deficiencies may operate in a number of ways so that the hæmatological changes are frequently so complex as to defy exact analysis.

Simple deficiency of vitamins, as in scurvy, or of internal secretions as in cretinism, may cause anæmia.

Clinical features.—When the deficiency results in no more than anæmia then pallor is usually the only obvious sign. Severe grades of anæmia cause dyspnœa on exertion and dilatation of the heart may occur. Splenomegaly is uncommon. When the deficiency is the result of some organic disease as in intestinal conditions, or has other far-reaching effects as with vitamin C deficiency, the anæmia is no more than a mere feature of the general clinical picture.

Hæmatology.—The nature of the hæmatological changes is entirely dependent upon the cause of the anæmia. Simple iron-deficiency anæmias are frankly hypochromic with a low mean corpuscular hæmoglobin concentration and colour index; poikilocytosis may be found as well as normoblasts; with superadded infection microcytosis may become prominent and the anæmia more marked by reason of reduction in the red cell count. When absorption deficiencies are complex the anæmia may be equally so from the hæmatological aspect though the majority of anæmias are hypochromic and microcytic with anisocytosis and macrocytosis occasionally appearing with liver principle deficiencies.

Iron-deficiency anæmia.—Iron-deficiency anæmias in infants past the milk-feeding period as well as in children are common among the poorer classes when the expensive iron-containing foods, such as vegetables, eggs and meat are beyond the power of purchase. The increased provision

of school meals has gone some way towards improving such conditions. The surveys of Davidson *et al.* (1935) in Aberdeen and in Edinburgh (1942) revealed a high incidence of iron-deficiency anæmia in children of low economic status; during the first two years of life only 17 per cent. of infants attained a normal figure. Likewise Mackay *et al.* (1943) and Davidson and Donaldson (1944) found a high incidence in children of school age. The simple iron-deficiency is often complicated by superadded infections to which such anæmic children are peculiarly liable.

Hypochlorhydria, which in itself is rare in infancy, may be associated with secondary infections and thereby contribute to the anæmia-producing factors (Ogilvie, 1935). Fullerton's (1937) series emphasizes the importance of superadded infection which may lead to a fall in hæmoglobin of as much as 50 per cent.

The *treatment* is to remove any primary and contributory causes and to administer adequate doses of iron on the same principle as in the nutritional anæmia of infancy.

Pernicious anæmia.—It is doubtful if true pernicious anæmia ever occurs in infancy and childhood. The failure in gastric secretion which induces the true disease does not occur in young subjects. Hotz (1924) points out that a " pernicious-like " anæmia in childhood is produced by diphyllobothrium infection, by syphilis and by gastro-intestinal causes; he emphasizes the rarity of cryptogenic cases of pernicious anæmia. It is certain that the natural macrocytosis of infancy (p. 1048) has sometimes been wrongly interpreted. Macrocytic anæmias are rare in childhood; when they occur they have usually an intestinal origin.

Cœliac disease.—Cœliac disease rarely causes the macrocytic or leucoerythroblastic types of anæmias which are occasionally found with adult idiopathic steatorrhœa. Neale, Smallwood and Shippam (1935) found no macrocytic cases, while Hardwick (1939) in an extensive review found that anæmia, if present, was almost always hypochromic and occasionally persisted in spite of treatment.

Iron is almost always required and may well be supplemented with small doses of liver extract. Despite the fact that the disease has certain features in common with sprue, the results of treatment with folic acid have been disappointing.

Scurvy.—Vitamin C appears to act as a general stimulus for cell metabolism and in the marrow, in the absence of the vitamin, the whole range of cells from endothelial cells to mature forms is affected. The anæmia is commonly normochromic but readily becomes hypochromic or even microcytic if hæmorrhages are extensive. Disproportionate slowing of maturation may occasionally produce macrocytosis. Anisocytosis is usual but poikilocytosis uncommon. Treatment with ascorbic acid results in a prompt reticulocyte response. Iron and liver extracts are not required unless the blood picture suggests that these substances are also needed. Copper should not be given for the anæmia of scurvy as this metal has a destructive action on vitamin C.

Cretinism.—The part played by thyroxin in erythropoiesis is not

fully understood ; it is believed to be a general marrow stimulant rather than a specific hæmopoietic factor. With cretinism the marrow tends to be hypoplastic and any associated anæmia is normochromic and normocytic. Iron deficiency may co-exist and iron treatment may improve the anæmia but a full and satisfactory response will not be obtained until the primary deficiency has been remedied.

Anæmias associated with constitutional diseases and infections

Constitutional disease and infections inevitably create a state in which malnutrition tends to become prominent. Consequently, anæmia is frequently associated with such diseases though the blood picture is in no way specific and the anæmia will rarely yield or even respond to anything other than the eradication of the primary cause.

Syphilis.—Anæmia, often of chronic hæmolytic type and associated with the von Jaksch syndrome, may sometimes be the only presenting symptom of congenital syphilis ; it may respond dramatically to specific treatment, the cure being completed by the administration of iron when iron deficiency is also a feature of the blood picture.

Rickets.—Rickets *per se* does not cause anæmia, nor is there any evidence that vitamin D has any specific hæmatinic action. The anæmia associated with rickets is frequently accompanied by the von Jaksch syndrome ; it is hypochromic and is relieved by the administration of iron, irrespective of the rachitic process.

Nephritis and nephrosis.—The interpretation of a blood examination in cases of nephritis associated with œdema is extremely difficult. The anæmia may merely become apparent due to a state of hydræmia and the figures should therefore be related to total blood volume before being assessed, whilst local œdema at the site from which the blood sample is taken should be excluded as far as possible. Though hydræmia may be a partial explanation of apparent anæmia, it is not a complete one, in that many who have massive œdema have no anæmia. The type of anæmia is very variable ; it may be normocytic, microcytic or sometimes macrocytic. In relation to this variability, the effect of acidosis or alkalosis on cell size should be borne in mind (p. 1048). The anæmia is intractable to ordinary hæmatinics. Anæmia is rare with nephrosis unless infection occurs, whereupon it may develop rapidly.

Rheumatism.—Acute rheumatic fever is associated with microcytic or microcytic hypochromic anæmia ; a macrocytic anæmia has occasionally been recorded. Cases of long duration may have a red cell count of half the normal figure with a low hæmoglobin and low colour index.

Endocarditis and pericarditis increase the anæmia. In the acute stage, there is usually a leucocytosis of 20,000 or more in proportion to the severity of the disease ; polymorphonuclears are the predominant cells and an eosinophilia has been commonly recorded, giving some support to the allergic theory of the cause of the disease. Often, however, there is no eosinophilia until convalescence. Arthritis, pleural effusion, peri-

carditis and endocarditis all increase the leucocyte count, whilst relapses are often preceded by the same phenomenon. Control of the fever by salicylates reduces the leucocyte count, but may also cause hypoprothrombinæmia (Meyer and Howard, 1942). The sedimentation rate is greatly increased in rheumatic fever and does not approach normal until some time after the fever has subsided. Subacute rheumatism manifested by recurrent tonsillitis, joint pains and mild chorea may have an apparently simple anæmia as the predominant and presenting symptom. It should be borne in mind that leukæmia may have an onset resembling acute rheumatism (p. 1094).

Acute specific fevers.—The hæmorrhagic types of acute specific fever are accompanied by anæmia, but the simple forms of these diseases do not greatly affect erythropoiesis. On the other hand, a number of fevers and infections give rise to well-defined leucocytic changes which are sometimes of value in diagnosis.

Rubella, at onset, is characterized by an absolute neutropenia and lymphopenia which, by the fifth day, has become an absolute lymphocytosis ; plasma cells, as many as 11 per cent., appear early in the disease often before the rash comes out ; they disappear after the first week, Türk cells are constantly present and reach a maximum about the fourth day.

Measles, likewise, shows neutrophil leucopenia at the time when the rash appears, whilst plasma cells and Türk cells are present fairly constantly though less often than in rubella.

Scarlet fever is characterized by a polymorphonuclear leucocytosis during the incubation and early stages of the disease and an eosinophilia during the recovery phases.

Whooping-cough.—The later stages of whooping-cough are associated with a definite, often a large, increase in total leucocytes caused almost entirely by lymphocytes which may comprise 60 to 90 per cent. of the count. Total counts of from 15,000 to 30,000 leucocytes per c.mm. are usual, but figures of 50,000 to 80,000 have been recorded, whilst Bourne and Scott (1922) reported a count as high as 176,000 per c.mm., and Newns and Pearson (1935) one of 150,000. Very young infants have, on the whole, somewhat lower counts than more mature children. Unfortunately, the characteristic blood changes are not found in the early catarrhal stage when leucopenia often occurs.

Glandular fever.—The form of the disease which most commonly affects children is acute in contrast to the subacute type found in adults. In the invasive phase, there is usually a polymorphonuclear leucocytosis of from 20 to 30,000 cells per c.mm., and in infants even higher figures may be encountered. The characteristic blood picture which follows consists of an increased leucocyte count with large numbers of so-called glandular fever cells, as well as a considerable increase in lymphocytes. In infants and children, the reactions may be entirely lymphocytic. Glandular fever cells resemble primitive monocytes in many respects. After the subsidence of the clinical condition the leucocyte count may not return to normal for many months.

Protozoan infections. Malaria.—The diagnosis of the acute disease by the finding of the parasites in the peripheral blood is relatively easy. The associated anæmia may be severe, for a single paroxysm may destroy as many as a million red cells per c.mm. In the chronic disease the diagnostic parasite may be difficult to find in either thin or thick smears of the peripheral blood ; sternal puncture samples are frequently positive, whilst the fairly constant reticulocytosis, as well as the leucopenic blood picture with monocytosis or pigment-containing monocytes are helpful diagnostic points.

Leishmaniasis.—Leishmania infection is fairly common among children in North Africa and Italy and in other parts of the Mediterranean littoral. The infecting parasite, often known as *L. infantum*, is similar morphologically to *L. donovani* and is probably identical with it. The disease has received the misleading name of infantile splenomegaly, but has a close clinical resemblance to kala-azar. The parasite may be found in the peripheral blood or more readily in splenic or marrow smears. The disease is accompanied by a progressive anæmia associated with a well-marked neutropenia.

Helminth infections.—Minor infections such as with oxyuris or trichocephalus usually cause no hæmatological disturbance. Eosinophilia is most marked with tæniasis, ankylostomiasis, ascariasis and trichiniasis. Some degree of anæmia may be associated with heavy ascaris infection ; with ankylostomiasis the anæmia may be severe. Diphyllobothrium infection which, in adults, is sometimes associated with a macrocytic anæmia resembling pernicious anæmia, rarely causes anæmia in the first decade of life (Birkeland, 1932).

Anæmia in children of school age

Primary disease of the erythron is extremely rare at school age. Most anæmias of this period are symptomatic. Furthermore, at this age, the vaso-motor system appears to be unstable so that anæmia is more apparent than real and mere pallor is an unreliable sign of anæmia. Perkins (1934) found that the blood count at this age shows considerable variation without apparent pathological cause. Poikilocytosis may be prominent after a period of work in school and then disappear rapidly after exercise in the fresh air.

Perkins divides the symptomatic anæmias of this age period into two classes. In the first are those associated with definite morbid processes and in the second those produced by general debility and malnutrition. Common morbid processes include subacute rheumatism and its various manifestations, tonsillar and dental sepsis. Less commonly a heavy infection with helminths may have the same effect. Latent tuberculosis may have to be considered when there is a persistent and intractable anæmia, but the disease is not common. Rarer morbid processes include congenital syphilis and late rickets, in both of which anæmia may be a prominent symptom.

General debility and malnutrition may be an inherited defect or the

result of previous severe illness. Actual starvation is rarely a cause of anæmia, but the quality of food eaten is of more importance than the quantity. This is well seen in the various surveys that have been carried out (p. 1061). Debility may readily be induced by lack of sleep and there can be little doubt that during summer months many children suffer in this way.

The endocrine disturbances and the increased iron requirements associated with puberty, especially the onset of the menstrual function in girls, readily contribute to an anæmic state.

Macrocytic anæmias

Macrocytic anæmias are rare in infancy and childhood. At birth there is a physiological macrocytosis which gradually disappears during the first month of life. Megaloblastic anæmias occuring in infancy have been reported by several authors. A description of the syndrome reported by Zuelzer and Ogden (1946) is given below.

It is extremely doubtful whether true pernicious anæmia ever occurs in infancy. Petersen and Dunn (1946) reviewed the literature up to 1942 and found only two cases which fulfilled all the criteria of true pernicious anæmia, whilst Benjamin (1948) in a later review could find only three proven cases of pernicious anæmia in children. He described another case first seen at twenty-one months, and followed up for a period of twelve years.

Hotz (1924), pointed out that a " pernicious-like " anæmia in childhood may be produced by diphyllobothrium infection, syphilis and gastro-intestinal causes. The latter include congenital malformations of the gastro-intestinal tract which interfere with the absorption of the hæmopoietic principle, post-operative shunts which by-pass portions of the intestines and acute and chronic diseases of the intestines, for example, cœliac disease, which interfere with absorption of the hæmopoietic principle. Occasionally severe liver disease, such as advanced cirrhosis, may be associated with macrocytic anæmia.

Megaloblastic anæmia of infancy

This macrocytic anæmia occurring in infancy was first described in 1946 by Zuelzer and Ogden in the U.S.A., and by Amato in Italy. It is characterized by a severe anæmia, normochromic and macrocytic in type; the bone marrow is megaloblastic. The condition responds to treatment with folic acid or liver extract and, unlike pernicious anæmia, has no tendency to relapse once the anæmia is cured.

Ætiology.—Since this condition has its maximum incidence in the first year of life when growth is most rapid and dietary deficiencies are most likely to occur, it is very likely that nutritional deficiencies, and possibly infections, play a part in the causation of megaloblastic anæmia. Aldrich and Nelson (1947), found a high incidence of vitamin C deficiency in infants suffering from this disease. This together with the work of

May *et al.* (1950), who produced a megaloblastic anæmia in monkeys similar to that occurring in infants, by feeding the animals on diets deficient in vitamin C, suggests that vitamin C deficiency may be an important factor in the production of the disease. Megaloblastic anæmia appears to be very much less common in this country, where vitamin C deficiency is nowadays rarely encountered.

It is unlikely, however, that this deficiency is the sole or chief factor. The megaloblastic dysplasia in the bone-marrow is identical with that which occurs in pernicious anæmia, indicating that the primary cause is a deficiency of the hæmopoietic factor. In contrast to pernicious anæmia, however, the deficiency is not permanent and once the anæmia is cured there is no relapse.

Symptoms.—The age of incidence is from birth up to eighteen months though occasional older cases are met with. Two of Zuelzer and Ogden's twenty-five cases were over eighteen months.
there is no relapse.

Fever, vomiting and diarrhœa are common at the onset and sometimes petechiæ. The chief clinical manifestation is extreme pallor. There is no enlargement of the lymph glands or of the spleen. When the anæmia has existed for several months, cardiac dilatation occurs and systolic murmurs may appear. Intercurrent infections are common.

Hæmatology.—There is a severe anæmia, normochromic and macrocytic in type. The hæmoglobin level may fall as low as 3 gm. per cent. with the colour index greater than 1. The Price-Jones curve is shifted to the right. There is an extreme degree of anisocytosis, many microcytes being present as well as macrocytes. There is no reticulocytosis but nucleated red cells are usually present.

There is a leucopenia with a reduction in the percentage of polymorphs. These tend to be larger than normal. The platelets are generally well below the normal level. In most cases a histamine-refractory achlorhydria is present.

The bone marrow shows a marked erythroid hyperplasia with many typical megaloblasts. In the myeloid series there are many large size polymorphs with hypersegmentation of the nuclei (macropolycytes).

Treatment with folic acid causes a rapid return to the normoblastic type of hæmopoiesis.

Treatment.—Folic acid or liver extract is specific. A reticulocytosis takes place four to five days after the start of treatment, and shortly afterwards the red cell and hæmoglobin levels begin to rise. There is also a rapid increase in the platelet count. A dose of 20 mg. of folic acid administered parenterally for seven to ten days appears to be sufficient. Ascorbic acid should also be given. As the anæmia is often severe blood transfusion may be necessary in neglected cases before specific therapy is started.

Sulphonamides and antibiotics should be administered whenever an infection is present.

THE HÆMOLYTIC ANÆMIAS

Erythroblastosis fœtalis

Under certain conditions of mating the fœtus or new-born infant may be affected by a serious and often fatal hæmolytic process, due to hæmolysins elaborated by the mother which pass back through the placenta and destroy the fœtal blood. The fœtus reacts to this destructive process with a result that a usual finding in the peripheral blood is a large number of erythroblasts. This feature has given rise to the general term *erythroblastosis fœtalis* to describe a group of clinically dissimilar conditions which have nevertheless a common cause and similar hæmatological changes.

The clinical groups include one in which the fœtus is greatly affected, often fatally, before birth, and therefore named *fœtal hæmolytic disease*, and one in which the disease becomes manifestly apparent at or soon after birth and therefore named *hæmolytic disease of the new-born*.

The sub-divisions of these two clinical groups are as follows :

Fœtal hæmolytic disease :	(1) Macerated fœtus with cirrhosis of the liver.
	(2) Hydrops fœtalis.
Hæmolytic disease of the new-born :	(1) Icterus gravis neonatorum.
	(2) Anæmia hæmolytica neonatorum (congenital anæmia).

Since all these clinical types have a common ætiology, pathology and hæmatology, they will first be described in general and the particular clinical features afterwards elaborated.

Ætiology.—The hæmolysis of the fœtal blood is due to isoimmunization of the mother by a corpuscular factor in the fœtus, which leads to the production of maternal hæmolysins ; these pass back through the placenta and destroy the fœtal blood. The factors involved are usually, but not always, the hereditary Rhesus (Rh) factors. The condition arises most commonly, in some 90 per cent. of cases, when the mother is so-called Rh-negative (rh) whilst the father and fœtus are Rh-positive (Rh). But the Rh factor is not a single entity and, in theory, erythroblastosis may arise whenever the fœtus contains a corpuscular antigen or antigens different from those found in the mother. Some 8 per cent. of cases fall into the class which involves the rarer Rh antigens and occasionally the A and B factors may be concerned in what is known as " heterospecific blood group pregnancy," that is, when the mother and fœtus are of different Landsteiner blood groups.

The isoimmunization theory implies a placental leak, so that the fœtal corpuscular antigen may enter the circulation. By analogy with other antigen-antibody reactions it can be assumed that the amount of leakage need only be small and once sensitized, the mother thereafter will react more vigorously to even small amounts of antigen. This is in keeping with clinical experience that the first-born may escape the

disease which subsequently becomes increasingly severe with each succeeding pregnancy. The isoimmunization theory therefore offers a rational explanation for three features of the disease, namely, its origin *in utero*, the family incidence and the increase in severity with each pregnancy.

Pathology.—As a compensation for the continuous blood destruction, there is a prolongation of or a reversion to an embryonic type of blood formation and the persistence or development of centres of erythropoiesis in the liver and spleen and sometimes in the kidneys, suprarenals, thymus, pancreas, pituitary body and lymph glands. These fœtal centres, which should ordinarily be inactive after birth, supplement the supply of cells from a highly active marrow. The liver may be greatly disorganized by the excessive blood destruction, being stained with bile, laden with pigment, cirrhotic or even necrotic. Bile staining of the basal nuclei of the brain (*kernicterus*) is common.

Hæmatology.—The anæmia is severe with a hæmoglobin as low as 3·45 gm. per cent. (25 per cent. Haldane): large numbers of early, intermediate and late normoblasts as well as reticulocytes are found in the peripheral blood. Occasionally, however, there is no erythroblastosis. The red cells are almost always macrocytic with much anisocytosis and poikilocytosis. Leucocytic changes are variable, but the commonest finding is a leucocytosis with a proportion of myelocytes and myeloblasts. Bilirubinæmia is constant. A low prothrombin content is common. Erythrophagocytosis by monocytes has been observed in the peripheral blood.

Prognosis.—It is not possible to predict the severity of the disease or its onset. Thus, the child may be born dead and macerated, or, it may appear normal at birth only to manifest severe hæmolytic phenomena a few days afterwards. The titre of the anti-Rh antibodies in the mother is no criterion of the severity of the disease in the fœtus; severe cases have arisen with low titres whilst, in many of the worst cases, no antibody or only an incomplete ("blocking") antibody can be demonstrated (Coombs' test) so that the titre (if any) may give an entirely false impression or may fail to predict the disease. Usually, however, the maternal antibody is present for several months before delivery and its passage to the fœtus must be continuous and increasingly potent during the last months of pregnancy. Mollison and Cutbush (1949) and others have demonstrated that the hæmoglobin value in the cord blood is a valuable index of the severity of the disease. Infants with a cord blood of 6 to 8 gm. per cent. are likely to die within twenty-four hours of birth, while those with a level above 15 gm. per cent. usually recover without treatment.

An important question is what prospects have a Rh-positive man and a Rh-negative woman of producing a normal child. Statistics show that the complication of erythroblastosis is by no means inevitable. The known distribution of Rh-positives in the population is 85 per cent. and of Rh-negative 15 per cent. From these figures about 13 per cent. of all marriages should carry the risk of erythroblastosis, but the disease arises in no more than 1 to 3 per 1,000 births. If the father be homozygous (Rh Rh) then all his children will be Rh-positive and potential candi-

dates for the disease, but if he be heterozygous (Rh rh) then one-half of the children should escape. Nevertheless, homozygous matings do not inevitably give rise to affected children, and it is not known why Rh-negative mothers do not always produce antibodies. More than one pregnancy may be required to induce an effective level; small families therefore influence the statistics available.

One other factor must be borne in mind, namely, that sensitization may be caused by transfusion. If a Rh-negative mother be transfused at any time with Rh-positive blood, she may form anti-Rh antibody and so increase her susceptibility to stimulation by a Rh-positive fœtus in a subsequent pregnancy. In these circumstances, not even a first-born child may escape the disease. Except in extreme circumstances a husband should never donate blood to his wife for should he possess antagonistic corpuscular antigens of any type the transfusion will sensitize the wife for future pregnancies.

Fœtal hæmolytic disease

Intra-uterine death may occur early and a macerated fœtus be delivered. Diffuse cirrhosis of the liver and gross splenomegaly in a fœtus with a voluminous pink placenta are characteristic features.

Hydrops fœtalis is rare. The infant is usually still-born or dies within a few hours of birth. The placenta is usually large and œdematous and often contains foci of erythroblastic activity. The serous cavities of the infant may be so distended with fluid that perforation is necessary in order to effect delivery. The liver and spleen are grossly enlarged and are the sites of active hæmopoiesis. The suprarenal cortex frequently shows lipoid infiltration. The heart may be twice its normal size. The blood may contain less than one million red cells per c.mm. with very large numbers of nucleated forms.

Erythroblastæmia may sometimes occur without the gross œdema so characteristic of hydrops fœtalis.

Hæmolytic disease of the new-born

Icterus gravis neonatorum.—The onset of the jaundice is usually within a few hours of birth and is rarely delayed beyond twenty-four hours. Parturition is generally normal, but if the vernix be a golden-yellow colour, the development of the condition may be anticipated. On the hereditary theory the disease is familial and successive infants are affected with increasing severity in the case of a homozygous male parent (p. 222); first- and second-born are more likely to escape than later infants. The mortality of the untreated disease is estimated at from 50 to 80 per cent. (McKinley, 1941). Permanent central nervous system lesions, arising from kernicterus (p. 1328) and causing athetosis and mental deficiency, may cripple about 10 per cent. of those who survive. Olive green pigmentation of the teeth some two and a half years after the original disease has been described (Ellis, 1938), whilst a generalized osteitis fibrosa has also been recorded (Braid, 1939). The liver and spleen are enlarged.

In cases which recover spontaneously the jaundice may disappear in two or three weeks or may persist for as long as two months.

The hæmatology is in principle that which is characteristic of the whole clinical group (p. 1068) but on account of survival certain manifestations of disordered hæmopoiesis may appear. Thus the indirect van den Bergh reaction is always positive, but the test may become diphasic from plugging of the bile ducts and destruction of liver cells; the urine and fæces contain a gross excess of urobilinogen. There is a hæmorrhagic tendency due probably to prothrombin deficiency which may be manifested by purpura, umbilical bleeding, melæna, hæmaturia or intracranial hæmorrhage.

Differential diagnosis.—The commonest cause of icterus in the new-born is physiological jaundice (see p. 221), which occurs to a lesser or greater degree in over 50 per cent. of births. This type of jaundice rarely appears before the third day of life and, except in premature infants, does not usually last more than seven to ten days. There is no enlargement of the liver or spleen and there is no anæmia; the Coombs' test is negative. Neonatal jaundice due to sepsis, once common, is now a rare phenomenon. Occasionally, however, icterus in the first week of life is due to septicæmia. Congenital obliteration of the bile ducts will give rise to progressive jaundice which does not usually commence until the second week of life. In neonatal hepatitis, jaundice may appear within forty-eight hours of birth. There is often a considerable degree of intra-hepatic obstruction, so that there may for a time be no bile in the stools. In this condition there is no splenomegaly, the blood cells are normal and the total blood bilirubin is at a high level.

Congenital hæmolytic icterus may give rise to jaundice within a few days of birth (Abt, 1940; Newns, 1951). The increased red cell fragility will establish the diagnosis.

Prognosis.—The mortality of the untreated disease is over 50 per cent. (Hawksley and Lightwood, 1934; McKinley, 1941).

With the introduction of transfusions with Rh-negative blood, as compared with blood unselected for Rh factors, a significant reduction in the percentage of babies dying has taken place. Gimson (1943), reported a series of eighteen cases which recovered after transfusion with Rh-negative blood. Diamond (1947), and Mollison and Cutbush (1948), describe groups treated with exchange transfusions in which the mortality was about 10 per cent.

Even so a proportion of the very severe cases die in the first two or three days of life, in spite of treatment. It should be remembered in assessing the results that a small number of cases of icterus gravis recover without any treatment. The level of cord-blood hæmoglobin is of importance in prognosis (p. 1072).

Anæmia hæmolytica neonatorum.—Such cases may exhibit severe anæmia within a few days of birth without either icterus or hydrops. But this form of the disease is rare during the first week of life and appears more frequently between the end of the first week and the age of two or three months. The later the onset the more mild and chronic the clinical

state. Pallor, rather than jaundice, draws attention to the condition. The spleen is always enlarged and there is an excess of urobilinogen in the urine. There is usually erythroblastæmia with reticulocytosis and anisocytosis, but macrocytosis is not so marked as in the more acute forms of the disease.

It should be borne in mind that marked erythroblastæmia is sometimes found in congenital syphilis and this possibility must always be excluded.

Treatment

In mild cases in which little damage has been done by maternal hæmolysins recovery is spontaneous and rapid, but in the majority this happy result cannot be confidently anticipated. In most cases appropriate blood transfusion must be given either by the exchange method (Appendix) or a single transfusion repeated if necessary. The intravenous route is to be preferred owing to the technical difficulty of infusing whole blood into the marrow cavity : with a previous history everything should be prepared for immediate transfusion of the newborn infant. At one time termination of pregnancy at the eighth month was advocated, in order to avoid the final month when maternal hæmolysins are likely to be most destructive. This is no longer practised.

The choice of donor has to be most carefully made. Complete investigation of red cell and plasma factors of the child and mother indicate the ideal type of blood to administer. Direct compatibility tests using a tube technique should always be performed. As a routine when the disease is known to be caused by anti-Rh antibodies the child should be transfused with Rh-negative blood of group O or of its own group. Suitable donors are more likely to be found among maternal than among paternal relatives. In an emergency, the red cells of the mother may be used provided they are freed from maternal plasma, washed and re-suspended in saline.

With rare and unusual antibodies, the washed red cells of the mother, provided they are compatible by the direct test, can be considered appropriate and safe. The volume of an orthodox transfusion recommended by Wiener and Wexler (1943) is 10 c.cm. per lb. of body-weight, *i.e.* 75 c.cm. for an infant of normal weight. This should be repeated on the second day. Assuming that all the infant's own cells are eventually hæmolysed, the transfusion of 150 c.cm. of blood ensures a hæmoglobin of 50 per cent. reckoning the blood volume to be 300 c.cm.

Exchange transfusion (replacement transfusion) is now widely practised especially in circumstances where a single transfusion is not likely to suffice. These include an urgent need to raise the level of hæmoglobin without increasing the blood volume ; the reduction to the minimum of the destruction of Rh-positive cells during the critical first four days of life, and the provision of such a concentration of Rh-negative cells at one operation that no further transfusions are needed. The technique most commonly used is to introduce a plastic catheter into the umbilical vein and make the exchange with a 20 c.cm. syringe which, by means of three way stopcocks, permits alternate withdrawal of infant's blood and infusion of donor's blood. The donor's blood is adjusted, by removal of

plasma, to have a red cell content of 5 to 6 million per c.mm. An amount of 400 to 500 c.cm achieves an exchange of the order of 80 to 90 per cent. The blood must be warmed. This method is only practicable during the first eighteen to twenty-four hours whilst the umbilical vein is patent.

Arnold and Alfred (1948) recommended cannulation of the saphenous vein in the groin the cannula being passed until it reaches the inferior vena cava. Wiener and Wexler (1949) employed a different technique. Blood was introduced into the saphenous vein at the ankle and the infant's blood was simultaneously withdrawn from the radial artery at the wrist. coagulation being prevented by the use of small amounts of heparin.

Controlled trials (Mollison and Walker, 1952) have shown that exchange transfusion offers a greater chance of survival than simple transfusion whilst the incidence of kernicterus is low with the former method. The good results from exchange transfusion, as compared with simple transfusion, were clearly demonstrated in two groups of cases: mature infants with a cord hæmoglobin below 11 gm. per 100 c.cm., and premature infants with a cord hæmoglobin above 11 gm. per 100 c.cm. The recovery rate of mature infants with a cord hæmoglobin concentration of over 11 gm. per 100 c.cm. is always high and kernicterus hardly ever occurs. Such cases do well with a simple transfusion given soon after birth. In premature infants with a cord hæmoglobin concentration below 11 gm. per 100 c.cm. the prognosis is bad, even when an exchange transfusion has been given.

The trials showed that premature induction of labour resulted in a slight reduction in survival rate as compared with the group who were allowed to go to full-term. Since premature infants are more likely to suffer from kernicterus (Allen *et al.*, 1950) than those which are full-term, it is clear that there is no justification for induction before term.

The Rh antibody may be present in breast milk in high titre and some recommend that breast feeding should be avoided. The majority believe that there is little evidence of definite harm and that the advantage of breast feeding should not be sacrificed. Heating or boiling the breast milk destroys the antibodies and this procedure is favoured by some.

HÆMOLYTIC ANÆMIAS OF LATER INFANCY AND CHILDHOOD

Acute, subacute and chronic hæmolytic anæmias

Excluding hæmolytic anæmias of congenital origin (p. 1069) there are a number of anæmias with hæmolytic features which exhibit a varying range of clinical severity. As to cause, these clinical types are to some extent divisible into those arising from definite hæmolysins demonstrable by the Coombs' test (p. 1068); those which are frankly secondary or symptomatic; those in which an overactivity of the reticulo-endothelial system especially the spleen (**hypersplenism**) is likely, and those in which no cause can be determined. The Coombs' test has provided an important means of differentiating the congenital hæmolytic anæmias in that the latter are

not usually associated with hæmolysins though the clinical features of both groups may be very similar.

The most dramatic type resembles the *acute hæmolytic anæmia of Lederer* as found in adults, though the blood picture may be modified by reason of the age-period. This form is rare and occurs between the ages of six months and three years. The onset is sudden with high fever. Severe anæmia develops within twenty-four to forty-eight hours accompanied by jaundice and usually hæmoglobinuria. Abdominal pains, diarrhœa and vomiting are common. As in the adult the disease has the clinical features of an infection but no causal agent has been found. The severe anæmia is often macrocytic and there is usually a considerable leucocytosis which includes a few myelocytes and many metamyelocytes. Empirical treatment with a carefully matched transfusion is often dramatic. Nevertheless, as in adults, a number of cases are due to hæmolysins which can be demonstrated by Coombs' test and these represent an acute phase of a hæmolytic anæmia which is more often subacute or chronic. Transfusion of cases with hæmolysins calls for much care in the selection of the donor in that the antibody has usually a wide range of action and the cells transfused will be rapidly destroyed if they themselves are capable of absorbing the hæmolysin. Splenectomy removes the probable source of the hæmolysin and has often to be undertaken in cases resistant to conservative treatment.

Most of the subacute and chronic hæmolytic anæmias of later infancy and childhood are *symptomatic* being frankly secondary to infective or toxic conditions such as septicæmia, syphilis, malaria, lead poisoning or drugs such as the sulphonamides, benzedrine and phenothiazone. Rickets and a nutritional anæmia are often associated but this disease cannot be regarded as a primary cause.

Other cases which have no apparent cause present a puzzling clinical group in which prognosis is difficult to estimate and treatment may have to be empirical or symptomatic. In some, hæmolysins can be demonstrated ; in others the main element may be hypersplenism as inferred from chronic hæmolytic symptoms and a marrow picture which is usually hyperplastic despite apparent aplasia of the peripheral blood.

Long custom has associated the name of von Jaksch with the syndrome which usually accompanies these relatively rare, obscure and often extremely chronic forms of anæmia.

The *clinical picture*, in the chronic case, is that of a well-nourished, pale, waxy-looking child between the ages of six months and three years, exhibiting splenic and hepatic enlargement, a severe hypochromic anæmia and often œdema and petechial hæmorrhages. Large abdominal veins may be present on a prominent abdomen. There is reticulocytosis, often erythroblastæmia, anisocytosis, poikilocytosis and, usually, a leucocytosis with a fair proportion of primitive cells. The van den Bergh reaction is usually an indirect positive and there is an excess of urobilinogen in the urine. The prognosis is not hopeless, but the illness may be lengthy and death from an intercurrent pulmonary infection is always a danger. If recovery takes place it is usually complete. The disease may disappear

spontaneously or may respond to hygienic measures, a nourishing diet and iron therapy; blood transfusion may be required. Splenectomy is rational if hæmolysins can be found or if hypersplenism is probable.

The fundamental pathology of these obscure anæmias is not understood. Some appear to be due to an overactivity of the reticulo-endothelial system which in itself may be the result of sensitization leading to the continuous production of hæmolysins. Differential diagnosis and the exclusion and elimination of any primary or contributory causes are the most important aspects. Syphilis may produce a similar picture whilst the exclusion of leukæmia by serial observations and by the examination of marrow samples is essential.

Hæmolytic anæmias due to a congenital anomaly

Congenital anomalies of the erythrocytes account for three types of hæmolytic anæmia of which the presenting features are anæmia, splenomegaly, bilirubinæmia and urobilinogenuria. In each case the blood picture is characterized by the presence of reticulocytes, and often nucleated cells, indicating a brisk reaction to the continuous hæmolytic process whilst the particular abnormal red cell peculiar to the type is the diagnostic feature.

(1) Congenital hæmolytic icterus—Synonyms: congenital hæmolytic anæmia; acholuric jaundice; acholuric family jaundice; familial spherocytosis.

(2) Mediterranean anæmia—Synonyms: Cooley's anæmia, thalassæmia; erythroblastic anæmia of childhood; target-oval cell syndrome.

(3) Sickle-cell anæmia—Synonyms: African anæmia; meniscocytic anæmia; drepanocytic anæmia, sicklanæmia.

Congenital hæmolytic icterus. Definition.—A congenital and hereditary chronic disease characterized by crises of excessive blood destruction, a constantly increased number of circulating reticulocytes, splenomegaly, microspherocytosis, increased fragility of the red cells and a variable bilirubinæmia, but with no bilirubin in the urine.

Ætiology.—The disease is inherited by males and females equally and may be transmitted by either. The hæmolytic tendency behaves as a dominant Mendelian character. Not all children of a family are necessarily affected. When only one child manifests the disease the forebears have probably been latent cases in whom the condition has been too mild to produce symptoms. The one fundamental variation from normal is the characteristic microspherocyte and all symptoms and manifestations, including increased fragility, are secondary to the spherocytosis. The spleen rapidly destroys the spherical cells, but it is improbable that a splenic factor is responsible for the microspherocytosis and fragility since neither of these is altered by splenectomy.

The subject may remain in a state of compensation until some additional factor such as an intercurrent infection causes a breakdown of the compensatory repair process and an increase in cell destruction.

Clinical features.—Symptoms may appear at any age even in infancy (Newns, 1951). At this age anæmia is a more pronounced symptom than jaundice and splenomegaly is usually of considerable degree (Abt, 1940). Most are diagnosed in late childhood or early adolescence. In some individuals neither jaundice nor anæmia may ever occur although microspherocytosis exists. Hæmolytic crises are a feature of the disease and these are often precipitated by an infection. In the latent periods between the crises the individual may feel comparatively well. At this time slight icterus may be present and an enlarged spleen may be felt. Lassitude and dyspnœa occur if there is much anæmia. Pain in the upper abdomen is a common symptom. The jaundice is never deep like that of obstructive jaundice. It is rather a lemon-yellow colour, which deepens during hæmolytic crises and may disappear entirely during remissions. Anæmia may occur without jaundice and jaundice without anæmia. In the latent period there may be neither jaundice nor anæmia, though an increase in the blood bilirubin can usually be detected. Splenomegaly is a constant finding. The spleen varies in size and is greatest during hæmolytic crises. Usually it is two to three fingers' breadth below the left costal margin. Even in latent periods it is generally palpable.

The urine is highly coloured and contains excess of urobilin and urobilinogen. Bile-salts are not present unless the common bile duct is obstructed by stones. The stools contain bile unless there is biliary obstruction.

Cholelithiasis is common in adult life but rare in children. The stones usually take the form of gravel. Retardation of growth and delayed ossification of bones are met with in severe cases in children.

Course.—Congenital hæmolytic icterus tends to be more severe in children than in adults. The quiescent course of the disease is interrupted by severe hæmolytic crises, whereupon the anæmia and jaundice increase and the spleen becomes large. These crises are usually initiated by an infection. Exceptionally they may cause death.

Diagnosis.—Congenital hæmolytic icterus should always be borne in mind when a child exhibits jaundice, anæmia and splenomegaly. A positive family history is very suggestive, and the presence of microcytic spherocytes in the blood is almost pathognomonic. The fragility test will clinch the diagnosis. Border-line cases with only slight increase in fragility present difficulty. The acquired forms of hæmolytic anæmia due to hæmolysins should be excluded with Coombs' test (p. 1068).

Hæmatology.—In a well-marked case the hæmatological findings are characteristic. The red cells are darker in colour and when examined in one plane are smaller than normal. Though the red cell diameter is small and the Price-Jones curve shifted to the left, the cells are not diminished in volume. For this reason, the mean corpuscular volume may be normal or even greater than normal. The mean corpuscular thickness and diameter-thickness ratio are increased. The blood film is characteristic. Some 20 to 30 per cent. of the cells appear as deeply staining microcytes against a background of normocytes and polychromatic cells (reticulocytes). Normoblasts are common particularly after a crisis,

whilst nuclear remains—Howell-Jolly bodies and Cabot rings—may also be found. Siderocytes are greatly increased. Rouleaux formation is irregular because the spherocytes do not fit snugly like normal cells.

The anæmia in a crisis is of the order of 2 to 3 million red cells per c.mm., whilst a constantly high reticulocyte count, from 5 to 50 per cent., is a feature of the disease both during a crisis and between.

A characteristic property of the spherocyte is an increased fragility to salt solutions. Normal red cells show no hæmolysis until the concentration of salt is reduced to about 0·45 per cent. and hæmolysis is complete at a concentration of 0·3 per cent. In congenital hæmolytic icterus the cells may begin to hæmolyse at 0·75 per cent. and the process be complete at 0·4 per cent. The test must be performed accurately and quantitatively under conditions of full oxygenation, otherwise mild forms of the disease will evade recognition by this crucial test. When the proportion of spherocytic cells is low the detection of the small fragile moiety is of first importance. The fragility may alter from time to time in the same patient; a single test is not therefore conclusive. The extent of the fragility is no indication of the severity of the clinical condition.

Pathology.—The spleen is considerably enlarged, is soft and deep red in colour, and engorged with blood. Thickening of the capsule and perisplenitis are not so common as in Mediterranean anæmia. Infarcts are rare. The pulp is congested. The follicles appear to be scarce because they are separated by the great mass of blood in the spleen. There is no thickening of the trabeculæ or reticulum. The bone-marrow is very hyperplastic, the yellow marrow being largely converted into red. There is marked hæmopoietic activity with large numbers of normoblasts. This hyperplasia is not so extreme as in Mediterranean anæmia and thinning of the cortex of the long bones is only slight. Pigment is deposited in various organs, chiefly the liver and spleen.

Treatment.—Medical treatment has little place in congenital hæmolytic icterus. Transfusion is indicated during a crisis if the red cells reach a low level. Cross matching has to be most carefully performed. Iron may be given during the recovery stage.

The only curative treatment is splenectomy. The decision to perform this operation will be influenced by the severity of the disease, the persistence of anæmia during the latent periods, the frequency of hæmolytic crises and the age of the patient. The operation is best carried out in the latent periods when the erythrocyte level is at its highest. Under modern conditions the mortality from the operation is slight, especially if the operation can be postponed until after the age of eight. Splenectomy is followed by permanent remissions of symptoms although increased fragility of the red cells, microcytosis and spherocytosis persist. Reticulocytosis and bilirubinæmia subside, indicating the disappearance of excessive hæmolysis. An increase in the number of red cells, platelets and leucocytes occurs after splenectomy, but after a variable period the level of these cells returns to normal.

Mediterranean anæmia. Definition.—A disease, almost always fatal when manifested in early life, having a familial and racial incidence,

characterized by progressive anæmia, splenomegaly and certain bony changes. The blood contains thin red cells known as leptocytes together with target cells, elongated cells and erythroblasts.

ÆTIOLOGY.—The disease is thought to be due to an inherited anomaly of the erythron which gives rise to leptocytes, target cells and elongated cells. The trait is found in the Mediterranean races and is the equivalent of the sickle-cell trait in negroes (p. 1078). The disease is familial and is apparently transmitted as a Mendelian dominant through either parent. It has been suggested that children who manifest the severe and fatal form of the disease, originally described by Cooley, are homozygous individuals inheriting the trait from both parents. Heterozygous children are thought to exhibit the mild forms which may be symptomless or give rise to no more than mild anæmia in childhood or adult life. Such cases nevertheless can be shown to have the leptocyte trait. Constant destruction of the abnormal cells gives rise to anæmia, bilirubinæmia, urobilinogenuria and splenomegaly.

CLINICAL FEATURES.—Cases vary considerably in severity; only the most severe ones are recognized in infancy. Pallor and fatigue are early symptoms, but they have usually been present for some time before medical aid is sought. Enlargement of the abdomen is sometimes the earliest noticed symptom. Progressive anæmia occurs with the gradual development of dyspnœa and palpitation. The heart becomes enlarged and hæmic murmurs appear. Growth is considerably retarded and the children are stunted.

The facial characteristics are not manifest until the disease has been in progress for some years. There is thickening of the malar bones, and also the bones of the orbit. The latter causes the eyes to be prominent and slightly slanting. This with the peculiar yellowish tint of the skin gives a somewhat mongoloid appearance. The colour of the skin is quite striking. At first pale, it gradually assumes a muddy sub-icteric tinge. Frank jaundice does not occur. The spleen enlarges early and eventually approaches the size of the spleen in chronic myeloid leukæmia. The liver also becomes enlarged.

COURSE.—This is progressive although there may be remissions and exacerbations. There are no hæmolytic crises such as occur in congenital hæmolytic icterus. Few patients survive the tenth year of life. According to Cooley only one person has been known to reach maturity. Death may be due to intercurrent disease or to exhaustion and anæmia.

X-RAY CHANGES.—The cortex of the long bones is thinned as the result of pressure by the hyperplastic bone-marrow. The X-ray picture shows transparency of the bones and medullary trabeculæ. These changes appear later in the pelvis, scapulæ and even the vertebræ. Spontaneous fractures have been reported by Blackfan. After some years the skull also shows characteristic changes. The bones of the vault become thickened and appear porous. Later bony spicules appear extending up from the inner table.

HÆMATOLOGY.—Mediterranean anæmia should be considered in any child of Mediterranean origin who has anæmia, leucocytosis and splenomegaly. The anæmia is of the order of 2 to 4 million red cells per c.mm.

with a hæmoglobin of from 4 to 9 gm. per cent. The anæmia is microcytic and hypochromic with a low colour index. The most striking feature is the large number of normoblasts which may be as many as 200 per 100 leucocytes. Anisocytosis is very marked giving a Price-Jones' curve of broad base ; poikilocytosis is also present. Target cells, elongated cells and oval cells are characteristic ; the cells are very thin and appear like pale discs. There is usually a persistent leucocytosis of from 15 to 50,000 leucocytes per c.mm. with a few myeloid cells in the more severe cases.

The shape of the cells is the antithesis of that found in congenital hæmolytic icterus : consequently the saline fragility test shows an abnormal resistance. Occasionally hæmolysis is not complete even in saline concentrations as low as 0·2 per cent.

The indirect van den Bergh reaction is positive and the icterus index raised.

Pathology.—The spleen is grossly enlarged with a smooth surface. The colour is rusty-red. Thickening of the capsule with perisplenitis is common. There is a diffuse increase in connective tissue. There is no marked phagocytosis or deposit of iron-containing pigments. Myeloid metaplasia is inconstant.

The liver has a cut surface which is a dark red-brown colour. There is fatty degeneration of the cells of the central part of the lobule. According to Whipple these contain an iron-free pigment, whereas in the cells in the peripheral part of the lobule an iron-containing pigment is found. The Küpffer cells also contain an iron-free pigment. There is no phagocytosis but there may be some centres of hæmopoiesis.

In the bones the cortex is thinned. The cavities of the long bones and the ribs are widened and filled with chocolate-red marrow. There is a remarkable degree of normoblastic activity. Phagocytosis is present, the phagocytes containing mostly iron-free pigment. There is a widespread development of bony spicules everywhere in the marrow cavity reaching its most striking degree in the calvarium.

The lymph glands are enlarged and show pigmentation. There is a widespread infiltration of the tissues, generally with pigment, resembling that seen in hæmochromatosis.

Treatment.—Iron, liver extract, and other hæmatinics have no effect, whether given by mouth or intramuscularly. Transfusions may be given during exacerbations but are purely palliative. Splenectomy has been frequently performed but no obvious improvement follows the operation. A striking result of the operation is the great and persistent increase in the number of circulating nucleated red cells of all types.

Sickle-cell anæmia. Definition.—A severe hæmolytic anæmia occurring almost entirely in negroes in which the red cells under appropriate conditions show a peculiar sickle shape. The anæmia exhibits remissions and exacerbations which are associated with abdominal and joint pains.

Ætiology.—The disease is the most common blood dyscrasia of negroes ; it is mainly but not entirely confined to negroes and mulattoes. Sickle-cell anæmia is an hereditary and familial condition. The sickle trait behaves as a Mendelian dominant and is transmitted equally

by male or female. The trait does not always cause anæmia. The essential nature of the disease is unknown but the majority of the features can be attributed to destruction of the abnormal corpuscles by the spleen. A latent phase of the disease, in which the cells do not circulate as sickle cells, is much more common than an active phase.

Clinical features.—The onset is usually in childhood but rarely in infancy. It is generally insidious and the anæmia has, as a rule, been present for some considerable time before causing dyspnœa or weakness. Sometimes a hæmolytic crisis, precipitated often by an acute streptococcal infection or an intercurrent illness, first draws attention to the disease. At times of crisis the patient is usually febrile, the scleræ are often of a greenish-yellow colour and the spleen becomes enlarged. Hæmic murmurs are associated with severe anæmia.

The later manifestations of the disease which are found in adults occasionally appear in childhood. These include attacks of severe abdominal pain, sometimes due to splenic infarction, joint pains simulating rheumatic fever, ulceration of the legs, and cerebral symptoms such as coma or epileptiform convulsions. Some thinning of the cortex of the long bones from pressure by the hyperplastic bone-marrow occurs, but it is slight compared with that seen in Mediterranean anæmia. In long-standing cases there may be thickening of the skull bones, and occasionally bony spiculation occurs.

Course.—This is variable. The cases developing early in life seem to be the most severe. Some die during a hæmolytic crisis. Many, after a long period of years, seem to improve and undergo spontaneous recovery, but the sickling trait of course remains. This may explain why fewer cases are seen in adults than in children. Splenectomy has little effect on the course of the disease.

Hæmatology.—During an attack the red cell count is from one to three million per c.mm. with hæmoglobin proportionately reduced giving a colour index in the region of unity. A neutrophil leucocytosis of from 10,000 to 30,000 per c.mm. is usual. Polychromasia is a marked feature and reticulocytes may form 25 per cent. of the circulating cells ; normoblasts are commonly found. The fragility of the red cells is usually slightly decreased, in that the sickle cells are somewhat resistant to saline hæmolysis. Phagocytosis of the red cells by circulating monocytes is a fairly constant feature. There is a raised icterus index and a positive indirect van den Bergh reaction with increased excretion of urobilinogen.

The ordinary stained blood film does not reveal the sickle shape except in very severe cases. The phenomenon is best seen in a sealed preparation of fresh blood which is examined after a few hours or as long afterwards as twenty-four hours.

Pathology.—In children, the spleen is almost identical in appearance with that of congenital hæmolytic icterus. There is rather more fibrosis than in the latter disease. There is a moderate degree of capsular thickening and perisplenitis. The pulp is engorged with blood, but the sinuses are empty. Many sickle cells are present. By the time adult life is reached the splenic tissue atrophies and the organ shrinks in size.

Connective tissue nodules, appearing as rust-coloured granules, are scattered throughout the spleen ; they contain masses of pigment infiltrated with calcium and iron salts. There is some enlargement of the liver. The Küpffer cells are prominent. There is considerable deposition of pigment. The bone-marrow is hyperplastic and contains many normoblasts. Many sickle cells are present. Pigment deposits also occur in the lymph glands and kidney.

Treatment.—Transfusions are indicated in hæmolytic crises, and iron is useful in the recovery stage. Liver extracts are of little value. Splenectomy has no effect on the progress of the disease. Treatment, therefore, is purely palliative.

PURPURIC AND HÆMORRHAGIC DISEASES

Purpura or hæmorrhage may arise as the result of damage to the capillary endothelium with or without concomitant defects or alterations in one or more of the factors concerned with the coagulation of the blood. Damage to the capillary endothelium by poisons or the toxins of organisms is the main factor in causing the purpura found in the hæmorrhagic forms of the acute specific fevers, acute bacterial infections, drug poisoning, the large group of clinical conditions attributed to allergy and in scurvy. Platelet deficiency may be contributory in such conditions, and is an important factor in essential thrombocytopenia or in any primary disease in which the production of platelets by megakaryocytes is suppressed or hindered. Deficiency of prothrombin leads to a hæmorrhagic tendency in hæmorrhagic disease of the new-born, in obstructive jaundice and when the liver is grossly damaged. Serious disturbances of liver function may also affect the coagulation mechanism in other ways.

In other hæmorrhagic conditions such as hæmophilia the fundamental cause is usually attributed to a deficiency of some plasma factor.

Investigation of the hæmorrhagic states necessitates determinations of the blood platelets, bleeding time, coagulation time, prothrombin time and the capillary resistance test of Hess. In difficult and rare cases crucial information may be supplied by the prothrombin consumption test and by a determination of fibrinogen.

Symptomatic purpuras

The essential lesion in this large group is capillary endothelial damage ; if thrombocytopenia occurs it is only slight. Some of the commoner causes are as follows :

(1) **Infections.**—Severe purpura may occur in hæmorrhagic forms of the exanthemata, *e.g.* measles, smallpox, scarlet fever, and in severe intoxications, *e.g.* pyæmia and septicæmia. Purpura may also occur in the course of severe streptococcal infections.

(2) **Drugs.**—Certain drugs may produce purpura, *e.g.* quinine, potassium chlorate.

(3) **Cachectic states.**—Purpura may occur in marasmic infants. It is also seen in the later stages of malignant disease and tuberculous meningitis. The hæmorrhages are usually limited to the skin and are petechial in form.

(4) **Mechanical.**—Examples of this are epileptic convulsions and the paroxysms of pertussis.

Anaphylactoid purpura

This group is likewise symptomatic. There is in one variety a distinct resemblance to serum sickness. The allergic agent as a protein is distinct from such substances as drugs. The exciting factor may be an article of food in which case the purpuric symptoms disappear if that article is removed from the diet. Some have a bacterial basis. The streptococcus is often concerned, even if not causal, and a sore throat is a frequent precusor of a purpuric attack. Gairdner (1948) links the Schönlein-Henoch syndrome with acute nephritis, rheumatic fever, purpura fulminans and polyarteritis nodosa ; all have commonly a streptococcal basis. In most cases of anaphylactoid purpura no specific causal agent can be discovered.

Three main types may be distinguished but they frequently overlap, and a case may show the features of more than one group.

(1) **Simple purpura.**—In this type there is a purpuric skin eruption without any other manifestations apart from slight fever and some general malaise. The skin hæmorrhages may be petechial or may take the form of ecchymoses of varying size. They may disappear after a few days and not recur, or successive crops of petechiæ may appear over a period of several weeks. Further attacks may occur at a later date.

(2) **Schönlein's purpura.**—In this form skin purpura is associated with painful joints into which effusions may occur. These effusions are usually serous and not blood-stained. The joint symptoms may precede the skin hæmorrhages and in such cases it is difficult to exclude rheumatic fever.

(3) **Henoch's purpura.**—Besides skin hæmorrhage there is bleeding into the wall of the intestine giving rise to cramp-like abdominal pain and passage of blood in the stools. Difficulties in diagnosis arise when the abdominal symptoms precede the purpura, as the symptoms resemble intussusception. In the latter condition an abdominal tumour is palpable.

The duration may be several weeks ; the abdominal symptoms do not persist as long as the purpura.

Prognosis.—Good in all types. Fatal cases are rare. Recurrences are not uncommon.

Diagnosis.—Examination of the blood will distinguish symptomatic from thrombocytopenic purpura. The difficulties of diagnosis from rheumatic fever and intussusception have been mentioned. Careful attention to symptoms and physical signs will usually lead to a correct diagnosis.

Treatment.—Rest in bed and warmth are essential. Adrenaline or antihistamine drugs may reduce the exudations whilst vitamin P is said to be of value when administered in doses of 20 mgm. of citrin intra-

muscularly twice a week. Salicylates do not relieve the joint pains of Schönlein's purpura.

Thrombocytopenic purpura

This form of purpura may again be subdivided into —(*a*) Symptomatic ; (*b*) idiopathic.

In the symptomatic group the thrombocytopenia is a secondary phenomenon, and may be due to destruction of megakaryocytes by leukæmic infiltration of the bone-marrow, or by a similar infiltration with neoplastic tissue, or abnormal lipoid as in Gaucher's disease.

Thrombocytopenia also results from marrow aplasia, such as occurs in aplastic anæmia. Secondary aplasia of the bone-marrow may be due to the effect of poisons such as benzol or X-ray irradiation.

Idiopathic thrombocytopenic purpura (essential thrombopenia).—As the name implies, the ætiology is unknown, but several theories of its causation have been put forward. One is that there is a toxic action on the bone-marrow ; another that the spleen has an inhibitory effect on the formation of platelets. Yet another view is that the platelets are destroyed more rapidly than normal by the spleen, and this is the most widely held theory. It is supported by the results of splenectomy. Another factor must be an increased permeability of the capillary endothelium. The capillary resistance test (Hess's test or the Rumpel-Leede phenomenon) is positive in thrombocytopenic purpura. The cause of this increased permeability is unknown.

Clinical features.—The disease is rare in infancy and is commoner in later childhood. Thrombocytopenic purpura varies a great deal in its severity. Three more or less distinct types can be recognized.

(1) *Fulminating purpura.*—This type is rare. The bleeding is of sudden onset, in a person who has previously been healthy. There is profuse bleeding from skin and mucous membrane and there is usually severe internal bleeding as well. High fever and other constitutional symptoms are present. In spite of blood transfusions these cases are nearly always fatal.

(2) *Mild subacute type.*—In this form there are ecchymoses and sometimes bleeding from the nasal and buccal mucous membranes. The hæmorrhage is of short duration but may recur at intervals. Sometimes there is only one attack. The spleen is not usually enlarged.

(3) *Chronic recurrent type.* This is the most characteristic form of the disease. Periodic episodes of hæmorrhage occur. Bleeding is from several sites, ecchymoses and bleeding from the buccal and nasal mucous membrane being common. Hæmorrhage may also occur from the uterus, gastro-intestinal and genito-urinary tracts. Cerebral hæmorrhage is rare. Splenomegaly is variable. In some cases the spleen is considerably enlarged, and in others it is never palpable. The periods of hæmorrhage last for four to six weeks and then gradually subside. The intervening interval is variable.

Congenital thrombocytopenia is a very rare condition. About eighteen cases have been described. In all but one the mother had purpuric

tendencies. The platelet count is low. There are widespread petechiæ but no severe hæmorrhages. Most children recover.

DIFFERENTIAL DIAGNOSIS.—The first thing to do is to differentiate between the primary and secondary forms of thrombocytopenic purpura, and this is sometimes difficult. In aplastic anæmia there is a very severe anæmia and a leucopenia, besides the thrombocytopenia. In thrombocytopenic purpura there is no leucopenia. Leukæmia without leucocytosis may present considerable difficulty, but some immature lymphocytes can usually be found in the circulating blood. Bone-marrow biopsy may be necessary to establish the diagnosis. Diagnosis from hæmophilia is not difficult, as in this disease the coagulation time is markedly increased and the platelet count is normal.

TREATMENT. *Medical.*—Blood transfusion should be resorted to without delay if the hæmorrhage is severe. Some workers have claimed successful results from the injection of snake venom and anti-venin. These might have some influence on capillary permeability but are unlikely to affect the thrombocytopenia.

Surgical.—Splenectomy should be considered in all but mild cases, especially if the platelets remain at a low level. If the initial attack is severe or there are frequent recurrences splenectomy should be performed. The operation should be carried out in a quiescent period preferably when the platelet count is at its highest. It is advisable to precede the operation by a blood transfusion. In some cases the platelets return to normal levels within a few weeks of splenectomy and remain at that level, and no further hæmorrhages occur. In many, however, there is no more than a transitory rise followed by a fall to their previous low level. Nevertheless, the liability to purpura is usually checked though occasionally bleeding recurs.

Ligation of the splenic artery has been practised, but it has no advantage over splenectomy except perhaps where dense splenic adhesions exist making removal difficult.

Congenital absence of fibrinogen.—This is a very rare anomaly and only seven cases have been reported (Henderson, 1945). Diamond mentions three additional ones (1950). The first case was described by Rabe and Soloman (1920).

The condition affects both sexes in contrast to hæmophilia, with which it may be confused. Parental consanguinity is present in a high proportion of the cases. There is a strong hereditary factor. Four of the seven cases had an affected sibling. From the first few days of life, bruising and bleeding manifest themselves. No fibrinogen can be found in the blood plasma. For this reason the blood does not clot at all. The bleeding time is variable; in some of the cases it has been normal. In two of seven cases intermittent thrombocytopenia has been observed. The blood sedimentation rate is extremely low. A striking feature is the very low capillary resistance, which may be the reason why bleeding is precipitated by minimal trauma.

Four out of the seven cases reported have died. There is a great danger of fatal umbilical hæmorrhage within the first few days of life.

Treatment.—The bleeding may be arrested by transfusion with whole blood or plasma. Purified fibrinogen is now obtainable. It may be injected intravenously and will immediately check the hæmorrhage. The injection must be repeated every three or four weeks. Sufficient should be injected to raise the plasma fibrinogen level to 200 mgm. per cent.

Hæmophilia

Definition.—An hereditary disease affecting males but transmitted by females and characterized by a prolonged coagulation time and a life-long tendency to excessive hæmorrhage. Sporadic cases without a hereditary history are occasionally seen.

Ætiology.—Only males suffer from the disease which is always inherited directly through the mother, in whom the tendency to bleed exists as a Mendelian sex-linked recessive character. The cause of the defect in coagulation is unknown. The platelets appear to be qualitatively and quantitatively normal, but it is possible that the platelets do not disintegrate normally so that thromboplastin is not liberated in sufficient amounts. The agglutination of platelets, a necessary prelude to rupture, is retarded; Wright (1946) demonstrated a diminution in the stickiness of the platelets, which militates against proper agglutination. Extensive investigations suggest, however, that the platelets *per se* are not responsible for the disease which appears to arise from a congenital deficiency of plasma thromboplastin. This disturbs many other stages in the chain reaction involved in the normal clotting mechanism including platelet action. On the other hand Tocantins (1943) has shown that hæmophilic blood has a large anti-thromboplastin activity which suggests that the delayed clotting may be due to an excess of anti-thromboplastin. These two theories are not necessarily contradictory since there may be both excessive anti-thromboplastin activity and a deficiency of plasma thromboplastin.

Clinical features.—Symptoms of hæmophilia rarely appear in infancy. This may be partly due to the fact that babies are subject to much less risk from trauma. Fatal bleeding has, however, been reported following early circumcision. Persistent hæmorrhage frequently occurs from slight cuts or abrasions. Epistaxis may follow a slight blow on the nose. Slight trauma may cause widespread ecchymoses. Severe hæmorrhage may follow minor operations, *e.g.* teeth extraction or tonsillectomy. Effusions of blood into joints are common. The knee-joint, being most liable to trauma, is frequently affected. These joint hæmorrhages tend to recur, and as they never completely resolve, ultimately result in partial ankylosis. Internal hæmorrhages are common; intracranial hæmorrhages may follow a relatively slight head injury. Few hæmophiliacs survive early adult life and a large proportion die in childhood. Mild cases occur, however, and a patient may show considerable variation in the hæmorrhagic tendency from time to time.

Diagnosis.—This is based on the family history and the finding of a very prolonged coagulation time. Clot retraction is usually defective.

The coagulation time is often normal between the attacks of bleeding. The bleeding time and platelet count are normal, which readily differentiates hæmophilia from thrombocytopenic purpura. A rare cause of prolonged coagulation is congenital fibrinopenia but, unlike hæmophilia, the blood will not coagulate when thromboplastin is added to it.

Treatment.—In spite of many trials no drugs or preparations will consistently reduce the prolonged coagulation time and the tendency to bleeding. Vitamin K has no effect. Hæmorrhage can sometimes be controlled by compression combined with local application of thromboplastic substances, *e.g.* fibrin foam. Transfusion, with fresh blood, is the only assured method available for controlling hæmorrhage. The procedure may have to be repeated, as the effect is not maintained for more than a short time. One of the fractions of plasma, alpha-globulin, may eventually become available to be given in place of blood.

Pseudohæmophilia.—This is a syndrome, possibly not a single clinical entity, in which excessive bleeding occurs in males and females alike, due to a prolonged bleeding time. The causation is unknown. It has been suggested that the defect is a failure of retraction of the capillaries after trauma.

The syndrome occurs in both males and females and is transmitted through either sex. There is a definite hereditary tendency though sporadic cases are described. Estren *et al.* (1946) report eleven cases of their own and sixty-two cases from the literature.

The chief symptom is excessive bleeding into the skin and from the mucous membranes and viscera: for example, kidneys and uterus. Epistaxis is the commonest form of hæmorrhage. Post-operative bleeding is common.

The only abnormality in the blood is a prolonged bleeding time. The coagulation time is normal. The number of blood platelets is normal and clot retractility is normal. The prothrombin time and serum fibrinogen are within normal limits.

Treatment is unsatisfactory. Where the bleeding point is accessible, pressure and the application of fibrin foam may arrest the hæmorrhage. Transfusions may be given to replace blood loss but these do not stop hæmorrhage. Treatment with calcium, vitamin K, or ascorbic acid is without effect. Splenectomy is of no value.

Hæmorrhagic disease of the new-born[1]

The general picture includes all cases of bleeding unassociated with trauma in the first week of life, such as spontaneous external hæmorrhages, internal hæmorrhages of the gastro-intestinal tract and all intracranial hæmorrhages not of traumatic origin. Traumatic intra-cranial hæmorrhages due to birth injury are excluded. Nevertheless, it is probable that hypoprothrombinæmia plays a part in some types of traumatic intracranial hæmorrhage, especially when the major hæmorrhage is delayed until the second or third day. In these infants there has probably been

[1] See also p. 231.

some slight oozing of blood from the tentorium or elsewhere in the meninges at birth. When the blood prothrombin falls the hæmorrhage increases and may prove fatal. Estimations of the frequency of the disease vary. Clifford places the incidence at 1 in 250 births. Many exhibit no more than slight external bleeding.

Ætiology.—The main factor in the causation of hæmorrhagic disease of the new-born is the low blood prothrombin level during the first week of life which is about 25 per cent. of adult values at birth and may fall as low as 10 per cent. In premature babies the prothrombin level is even lower, thus explaining the increased incidence of neonatal hæmorrhage in premature infants. The usual prothrombin curve shows a low prothrombin value at birth, becoming still lower from the second to fifth day. Thereafter there is a gradual rise to normal values.

On the other hand some observers have found an increased prothrombin time at birth which gradually shortens during the first week, until by the second week it has become stationary. There is, therefore, some variability in the prothrombin curve during the first week of life as described by various workers, but it seems to be generally agreed that there is a physiological type of transient hypoprothrombinæmia of varying extent during the first three to six days after birth, and that by the second week the blood prothrombin has risen to a stationary level.

It has also been shown that an increase in the prothrombin level in new-born infants follows administration of vitamin K. The cause of the low prothrombin level in new-born infants has not yet been completely elucidated. Vitamin K is essential for the proper formation of prothrombin by the liver, and in the new-born there is a deficiency of vitamin K, which is ordinarily synthesized by the action of the intestinal bacteria on food. In the first two to three days of life the intestinal tract is sterile, but bacteria very soon appear after the ingestion of milk whereupon vitamin K synthesis begins. There must therefore be a delay of several days before enough vitamin K is formed to permit the production of adequate amounts of prothrombin.

Nevertheless, the explanation of the hæmorrhage is probably not as simple as this. Prothrombin values as low as 5 per cent. of adult levels have been found without hæmorrhage, whilst sometimes the prothrombin level has been no lower than in infants showing no hæmorrhage. This suggests that there may be some factor which interferes with the conversion of prothrombin into thrombin.

It is also probable that the permeability of the capillary endothelium is increased in hæmorrhagic disease since the hæmorrhages are spontaneous. The cause of this permeability is not known.

Symptoms.—The first symptoms appear as a rule on the third or fourth day, more rarely on the second day. The hæmorrhage is spontaneous and usually multiple. The common sites of origin are the gastro-intestinal tract (melæna and hæmatemesis), umbilicus, and nose, mouth and skin. Bleeding from the genito-urinary tract is uncommon. Cutaneous hæmorrhages often occur in places exposed to pressure.

The general condition of the infant will depend on the site of the

bleeding and its severity. When there is internal hæmorrhage rapid prostration and collapse ensues with all the symptoms of acute hæmorrhage, *e.g.* pallor, restlessness, dyspnœa, air hunger. Meningeal bleeding will result in rapidly developing coma. The bleeding seldom lasts more than three or four days and its cessation is often abrupt. Once hæmorrhage ceases there is no relapse.

Diagnosis.—Spontaneous bleeding may occur apart from hæmorrhagic disease. Cord oozing may be the result of infection. Pseudo-menstruation may be the cause of vaginal bleeding. Duodenal ulcer has been observed in the new-born and may give rise to severe melæna. Congenital syphilis occasionally causes bleeding from the cord or from the gastro-intestinal tract. Hæmorrhage may also occur in erythroblastosis.

Rare diseases like congenital fibrinogen deficiency and congenital thrombocytopenic purpura will give rise to hæmorrhage.

If these conditions are excluded the diagnosis is probably hæmorrhagic disease of the new-born. The diagnosis may be confirmed by estimating the prothrombin time by Quick's method.

Prognosis.—The disease is often fatal when there is internal hæmorrhage unless treatment is given early. External bleeding is rarely severe and recovery is the rule.

Treatment. Prophylactic.—The disease may be prevented by administering 1 mgm. of acetomenaphthone by mouth in the first twenty-four hours of life, thus preventing the post-natal fall of the blood prothrombin level. As vitamin K is transmitted to the fœtus *in utero*, it may be given to the mother: 1 to 2 mgm. of a water-soluble analogue should be injected intramuscularly in the first stage of labour.

Therapeutic.—External hæmorrhage may subside spontaneously or will stop rapidly on administration of vitamin K. When there is hæmorrhage from the gastro-intestinal tract, exsanguination of the infant is so rapid that blood transfusion is urgently necessary, especially as the new-born infant stands blood loss badly. Vitamin K should also be given, preferably intramuscularly, in doses of 1 to 2 mgm., which may be repeated after eight hours. Water-soluble analogues of the vitamin should be used, as oily preparations are very liable to cause abscesses. Intramuscular injections of whole blood are quite ineffective in stopping the hæmorrhage. Hay *et al.* (1951), describe the effect of vitamin K injections in pregnant women before delivery. There was a higher percentage of cases of hæmorrhagic disease in their babies than in those in a large control series.

APLASTIC ANÆMIA

Complete aplasia of the marrow is extremely rare especially as a primary disease. On the other hand some degree of hypoplasia ranging from mild states up to a degree where the whole clinical and hæmatological picture suggests almost complete aplasia is relatively common. The condition is almost always secondary to some noxious or toxic agent, though this may be extremely difficult to identify. Primary hypoplasia, and especially aplasia, is rare. A further group falls into the category of

hypersplenism and is characterized by a peripheral blood picture indistinguishable from the aplastic states. Yet examination of the marrow shows a hyperplasia of that tissue. This impotent hyperplasia is believed to be due to overactivity of the spleen and is rationally treated by splenectomy. Since the clinical course and the hæmatology of all the conditions are identical they will be described together.

Ætiology.—The cause of primary hypoplasia is unknown. Secondary causes include severe sepsis, exogenous poisons such as benzol, arsenobenzene, nirvanol, the sulphonamides and almost any drug to which an individual may develop a sensitivity. A similar condition may arise from over-dosage with X-rays or radium or from replacement of the marrow by infiltrating tissue or malignant growths as with sympathoblastoma, myeloma or lipoid material in Niemann-Pick disease or Hand-Schüller-Christian disease.

Pathology.—In principle the red-marrow is everywhere replaced by a cellular yellow marrow containing no centres of erythropoiesis or leucopoiesis and few megakaryocytes. The aplasia is rarely complete and many bones may contain single areas of active marrow.

The blood picture reflects the state of the marrow. The anæmia is normocytic and normochromic with no reticulocytes or nucleated cells and no anisocytosis or poikilocytosis. Leucopenia due to neutropenia may be very marked. Blood platelets are reduced in number.

Clinical symptoms.—The onset is usually insidious. Early symptoms are dyspnœa and palpitation of the heart due to the severity of the anæmia. Hæmorrhagic manifestations, resulting from the profound thrombocytopenia often draw attention to the hitherto unsuspected disease. Hæmorrhage is persistent and severe and since the bone marrow is unable to repair the blood loss the anæmia increases. Bleeding is commonest from the mucous membranes of the nose and mouth. The patient has a waxy pallor without any icterus. There is no enlargement of the spleen or lymphatic glands. Death is usually the result of heart failure or intercurrent infection to which the patient suffering from aplastic anæmia is peculiarly liable owing to the severe neutropenia. The primary disease is progressive without remissions and is invariably fatal, though sometimes the course is a long one.

Diagnosis.—A combination of severe anæmia, leucopenia, thrombocytopenia, without any signs of blood regeneration is very suggestive of aplastic anæmia. Differentiation from aleukæmic leukæmia may present great difficulty. In leukæmia there is almost always some enlargement of the spleen and commonly some degree of lymphadenopathy. The blood picture tends to be more variable. Nucleated red cells may be present, and there is usually to be found an occasional immature white cell. The results of a bone-marrow biopsy are usually decisive since in leukæmia there is an infiltration of the marrow with immature white cells.

Treatment.—All primary causes must be explored and eliminated. Direct efforts to stimulate bone-marrow function by means of iron, liver,

pentose nucleotide or yellow bone-marrow usually fail. Proteolysed liver is sometimes effective. Folic acid is worthy of trial as it is occasionally successful in certain anæmias which are refractory to liver extract. Transfusion will temporarily relieve the anæmia and arrest the hæmorrhage, but its effects are transient. Repeated transfusions may keep the patient alive for a time. The grafting of bone-marrow has been claimed to be successful in some cases. Splenectomy is rational when the marrow picture conforms to that found in hypersplenic states (p. 1088).

Congenital hypoplastic anæmia.—This may be regarded as a less severe form of chronic hypoplasia; it occurs at or soon after birth and involves mainly the erythropoietic tissue of the bone-marrow. Diamond and Blackfan (1938) reported four cases, and a number have been described since (Rubell, 1942; Robson and Sweeney, 1948; Cathie, 1950). The condition is characterized by a slowly progressive anæmia beginning in early infancy without any hæmorrhagic tendency. There is only a moderate leucopenia. Small and poorly formed reticulocytes are present in the circulating blood. The bone-marrow shows a moderate degree of hypoplasia. There is no obvious reduction of granulocytes or megakaryocytes, but there is a moderate hypoplasia of the erythropoietic elements. The patients of Blackfan and Diamond were given frequent blood transfusions at intervals of six to twelve weeks. They kept in relatively good health and developed normally. These children do not appear to be abnormally susceptible to infections. They are able in a remarkable degree to adjust themselves to the low hæmoglobin level. The spleen is not enlarged at first but both it and the liver later enlarge owing to iron deposits following the repeated transfusions.

The *ætiology* is obscure. There is no evidence of infection or of an endogenous or exogenous toxin. Two theories of its origin have been put forward.

(1) There is a congenital deficiency of red marrow tissue which is unable to replace worn-out red cells.

(2) There is an inborn error of metabolism of some of the blood-building substances, which may produce a deficiency state leading to anæmia.

Treatment.—Repeated blood transfusions at intervals of six to eight weeks will correct the anæmia. Splenectomy was performed in two of Blackfan and Diamond's cases. One was improved and still alive one year later. No effect was observed on the other.

Fanconi's syndrome

(FAMILIAL APLASTIC ANÆMIA WITH MULTIPLE CONGENITAL DEFORMITIES)

In 1927 Fanconi described three brothers aged five, six and seven, who had a severe aplastic type of anæmia, which was refractory to treatment. There was also leucopenia, and thrombocytopenia. A number of congenital deformities were present, namely microcephaly, hypoplasia of the testicles, congenital strabismus and a generalized brown pigmentation of the skin. All three patients died.

The condition is a rare one. Further familial cases have been reported by Weil (1938), in two out of five children, by Hyorth (1940), in brother and sister, and by Dacie and Gilpin (1944), in two brothers. Sporadic cases have been described by Weil (1938), Ühlinger (1929), van Leuwen (1933), Estren and Dameshek (1947), and Beautyman (1951).

The ætiology of the syndrome is not known. Fanconi postulated that it was an inherent chromosome defect.

Symptoms.—There is progressive pallor, which may reach an extreme degree. Subjective symptoms such as dyspnœa and weakness are often strikingly absent, since the child is able to adjust himself to the low hæmoglobin level. Hæmorrhagic manifestations are common, such as bruises, petechiæ and hæmorrhages from mucous membranes. Owing to the marked neutropenia intercurrent infections are liable to occur. There is usually some retardation of growth.

Examination of the blood reveals a normochromic anæmia, leucopenia and a marked thrombocytopenia. Reticulocytes are scanty. The bone marrow changes are those of a hypoplastic or aplastic anæmia and are progressive.

The developmental abnormalities most commonly affect the bones of the forearm and hand, the eyes, the kidneys and the gonads. Dacie and Gilpin's fatal case had a horse-shoe kidney. One or two cases have had cardiac abnormalities.

The prognosis is grave. Most of the children reported have died though they have been kept alive for varying periods by means of repeated blood transfusions. One of Dacie and Gilpin's cases is still alive after several years' observation.

Treatment.—There is no specific treatment. Frequent blood transfusions will keep the patient alive for a time but some have developed cardiac failure and died.

Splenectomy has been performed in several cases. In one of the cases of Dacie and Gilpin and the case of Estren and Damashek, there was considerable improvement.

Agranulocytosis

The phenomenon agranulocytosis, which consists of a marked leucopenia due to extreme reduction or absence of cells of the myeloid series, is almost always due to some toxic factor, though the exact cause may be difficult to establish. The rare idiopathic primary form is assumed to be due to an essential aplasia of the myeloid tissue, and may be associated with aplasia of the other bone-marrow elements (p. 1088).

By reason of the lack of granulocytes, the patient is unduly susceptible to infection and ulceration, usually manifested in the mouth and pharynx, so called agranulocytic angina; sometimes there may be recurrent skin lesions.

Clinical types.—The condition may be acute, fulminating and rapidly fatal; more commonly it is subacute or chronic and relapsing and occasionally recurrent in a regular cycle. A distinctive type, known as *primary splenic neutropenia*, has been described by Wiseman and Doan (1942).

In this there is moderate splenomegaly, in addition to the agranulocytosis, and occasionally purpura, due to thrombocytopenia, with or without hæmolytic anæmia. This form is attributed to overactivity of the spleen and responds well to splenectomy.

Causes.—Numerous toxic drugs, to which an individual may be unduly sensitive, are known to cause agranulocytosis. The list includes analgesics of the amidopyrine group, sulphonamides, arsenic and other metals, benzol derivatives, thiouracil, phenacetin and acetanilide. Agranulocytosis may also arise from damage to the bone-marrow caused by excessive doses of X-rays, radium and radioactive isotopes, as well as from the toxins of a severe and overwhelming infection, together with certain chronic infections, such as congenital syphilis.

Treatment.—The main object of treatment is to prevent or deal with the secondary infection to which the patient is unduly susceptible. This, together with the removal of any suspected primary cause, allows the marrow to recover. The use of leucocytic stimulants, such as nucleic acid, pentose nucleotide, liver extract and folic acid has little success. These stimulants are effective in normal persons, and in those whose neutropenia is largely due to a nutritional deficiency; they have little or no action, and often an unpleasant reaction in toxic and infective states.

A regular course of penicillin, or other antibiotic, in full dose is the best method of controlling infection. Aureomycin or chloramphenicol may be required in penicillin-resistant cases.

LEUKÆMIA IN INFANCY AND CHILDHOOD

Definition.—A fatal disease characterized by an abnormal proliferation of the leucopoietic tissues which usually results in the appearance in the blood of large numbers of leucocytes, of which many are immature.

Ætiology.—Leukæmia is considered by some to be the result of "infection." In mice lymphatic leukæmia has been transmitted in series by injections of blood. Intravenous injections of leukæmic blood into human patients have not caused the disease. All attempts to transmit the blood by blood or tissue to lower animals have failed.

The view most widely held is that leukæmia is a malignant neoplastic process. The rapid growth of leukæmic cells, the progressive nature of the disease, with the inevitably fatal outcome, are very like malignant disease. Certain types like chloroma seem to be midway between leukæmia and a neoplasm.

On the other hand, the dissemination and spread of leukæmic cells are not at all like a neoplasm which starts as a local tumour, and later gives rise to metastases.

The work of Israels (1940) and Hoogstraten (1949), however, has shown that leukæmic cells when cultured *in vitro* develop into normal cells and preserve their power to differentiate unlike cancer cells, which, *in vitro*, go on producing malignant cells. This suggests that, in leukæmia, there is some humoral factor, which acts, *in vivo*, on the leucocytes, causing them to grow in an abnormal manner.

There have been rare human examples of leukæmia in families. Petri (1933) and Decastello (1939) reviewed this matter; the former found thirty-three cases of familial leukæmia, of which 11 appeared to be incontrovertible. The evidence for the direct transference of the disease in the human subject is not sufficiently strong to exclude coincidence. Kelsey and Anderson (1939) reviewed the congenital aspect and accepted nine authentic cases, of which eight were myeloid and one lymphatic. Ward (1917) and Grier and Richter (1939) studied the relation between leukæmia in infants and mothers and found nothing to support an infective origin. Thus a leukæmic mother gave birth to healthy children, and no infant developing leukæmia in the first few months of life had ever had leukæmic parents.

Types and age-incidence.—Leukæmia in childhood is most common during the first four years of life; it may occur in infancy. Occasional cases appearing in the neonatal period have been reported. The incidence steadily declines from the age of eight onwards and is rare during adolescence. The average duration of life is two to four months; the leukæmic process is therefore usually acute. Ramsey (1927) in reviewing one hundred cases of leukæmia in infancy and childhood found that seventy-five per cent. were of lymphatic type. Gittins (1933) in a study of fourteen cases of leukæmia in children found eleven lymphatic, two myeloblastic and one monocytic; in this series the counts were often aleukæmic. It is probable, however, that the myeloid type is more common than is supposed.

Myeloid leukæmia as found in the adult, is relatively rare; in the young, when the myeloid series is involved, the disease is usually of the acute myeloblastic type with an average cell count of 50,000 per c.mm. The monocytic type is rare. Court and Edward (1939) describe two examples and review twenty-three authentic cases previously reported; they found the age incidence of this type usually above five years. The initial phases of leukæmia in childhood may be very insidious from the clinical aspect, especially when the disease is not obvious from an examination of the peripheral blood (aleukæmic leukæmia, p. 1097). In childhood a severe and intractable anæmia accompanied by neutropenia calls for a marrow puncture examination in order to exclude leukæmia, whatever the total leucocyte count may be.

Hæmatology.—Anæmia is always a marked feature; it is usually normochromic and normocytic, but is occasionally slightly macrocytic; anisocytosis and poikilocytosis are not usually prominent. The red cell count is commonly of the order of 1 to 2 million per c.mm. and may be less in the terminal stages. As to the leucocyte count, the more chronic the process, the higher the count; with the acute disease and in the terminal phases of the chronic types, the count is usually low. Aleukæmic types or phases are common and in these a marrow biopsy may be essential in order to establish the diagnosis. Frank cases with a marked leucocytosis and many primitive cells present no difficulty. Intermediate and aleukæmic cases have to be distinguished from the striking hæmatological reactions to various infections which may be found in the young, whilst

the normal lymphocytic predominance of infancy has to be borne in mind. In differential diagnosis, association of a severe anæmia with suspicious blood changes is an important point. In the young, certain features of myeloid leukæmia can be closely imitated by an intense inflammatory reaction, but in the latter case there is usually relatively little anæmia.

Likewise, in whooping-cough, the lymphocyte count may run into tens or even hundreds of thousands per c.mm. (Pearson and Newns, 1937), whilst the lymphocytosis and monocytosis of glandular fever may be a source of difficulty.

Pathology.—The morbid anatomy does not differ greatly from that found in the adult disease, save that macroscopic focal leukæmic deposits in the viscera rarely occur in children; the infiltration is usually diffuse (Gittins, 1933). Leukæmic infiltration of bone and joint tissue is relatively common. In the spleen, infarcts, perisplenitis and adhesions occur. In the lymphatic type, the spleen is homogeneous and no Malpighian bodies can be discerned; the whole tissue consists of densely packed lymphocytes; subcapsular hæmorrhages may be present; the liver is usually moderately enlarged owing to collection of lymphocytes in the portal tract. The skin sometimes shows localized swellings of infiltrating lymphoid or myeloid masses.

Clinical features.—Leukæmia in children may be acute or chronic. A few cases may be classed as subacute. The great majority of the cases met with in children are acute with a course lasting less than six months from the onset. Acute leukæmias may be lymphoblastic or myeloblastic. The cell present in the bone-marrow and the blood is usually an early lymphoblast or myeloblast. Occasionally it is impossible to say to which series the type cell belongs and it is then sometimes designated a stem cell.

Whatever the nature of the leukæmic cell present in cases of acute leukæmia the clinical features are the same and a single description will cover all types.

The *earliest symptoms* are generally pallor and asthenia. Other early symptoms are enlargements of glands in the neck and skin hæmorrhages. Enlargement of the abdomen is usually quite a late symptom.

Pallor and asthenia.—These symptoms are insidious in onset and pallor has usually reached a considerable degree before the parents take much notice of it. The child begins to show undue lassitude and tiredness, does not want to do anything active and wants to lie about most of the day; at the same time there is gradual onset of pallor of the skin and mucous membranes. In the later stages anæmia is rapidly progressive and the pallor becomes very striking.

Enlargement of lymph glands.—This is relatively slight in degree compared with that met with in the chronic leukæmias. There is usually, however, some enlargement of lymphatic glands, especially in the neck. The glands are soft and mobile and occur in clusters. Enlargement of the axillary and inguinal glands may also occur but there is not much enlargement of the internal glands, *e.g.* in mediastinum or abdomen. They do

not reach a sufficient size to produce pressure symptoms. In a personal case of acute leukæmia the child had abdominal pain and was operated on for appendicitis. The appendix was normal but the ileocæcal glands were enlarged and dark purple in colour and on section were found to be packed with lymphocytes, the normal structure being destroyed. A blood count a few weeks later showed a leukæmic blood picture. Occasionally the salivary glands are infiltrated and enlarged (Mikulicz's syndrome).

Hæmorrhages.—Blood platelets fall to a low level in acute leukæmia and hæmorrhages are to be expected. These may be confined to the skin and may be purpuric, giving rise to ecchymoses of varying sizes or petechial bleeding from mucous membranes, the common sites being the mucous membranes of the nose and mouth (gums).

Hæmorrhage from the tonsils, which are often enlarged, is frequent. Hæmorrhage may also occur from the gastro-intestinal and urinary tracts and occasionally into the retina. In the fulminating type of acute leukæmia when the total course may not be more than six to eight weeks, profuse hæmorrhage from mucous membranes may take place and may be the salient clinical feature, giving rise to a rapidly progressive anæmia.

Splenomegaly and hepatomegaly.—The spleen is enlarged though never to the extent met with in the chronic leukæmias. It is soft in consistency and, unless carefully felt for, may be easily missed. It must be remembered that in young children the spleen tends to enlarge downwards, rather than towards the mid-line. It should be felt for much farther out than usual, almost in the loin.

In a rare type of case the spleen is not palpable until the terminal stages when it may begin to enlarge. Such cases usually have a leucopenic blood picture. The liver is usually slightly enlarged but rarely attains any great size.

Fever.—There may be no fever but sometime in the course of the disease there is usually an irregular low pyrexia. High fever is occasionally seen even in the absence of intercurrent infection.

Stomatitis.—This occurs in about 10 per cent. of cases and is accompanied by secondary infection. The gums are swollen, bleeding, and on pressure pus exudes. Vincent's spirochæte and fusiform bacilli are commonly found in the exudate.

Limb pains.—Sharp lancinating limb and joint pains are not infrequent, and may lead to an erroneous diagnosis of rheumatism or rheumatoid arthritis. Examination reveals no abnormality and X-ray may or may not show skeletal lesions.

Abdominal pain sometimes occurs. It is usually of a colicky nature and is occasionally quite severe. It may be referred to the umbilicus or to the right iliac fossa, when appendicitis may be suspected.

Skin.—Leukæmic infiltrations of the skin are rare in acute leukæmias. When present they form nodules about the size of a pea but may increase slowly in size and develop a necrotic centre.

Rarely *neurological* complications are met with. These are due to the

occurrence of small masses of leukæmic cells in the spinal canal, which exert pressure either on the spinal cord or the nerve roots. The symptoms vary with the site of the infiltrations but may simulate a transverse myelitis. The *basal metabolic rate* has been shown to be persistently high in leukæmia.

Radiological changes.—These are not uncommon. Silverman (1948) found X-ray changes in 52 out of 103 leukæmic children. Four types of lesions are met with; transverse bands of diminished density, osteolysis, osteosclerosis, and subperiosteal new bone formation.

Course.—Acute leukæmia is invariably fatal and its course is rapid and progressive. Death usually occurs within six months of the onset and often within three months of diagnosis. Natural remissions occasionally occur and blood transfusions may bring about a temporary improvement.

Remissions of varying duration may also follow treatment with aminopterin and similar substances, and with ACTH and cortisone.

Differential diagnosis.—The diagnosis of leukæmia is chiefly based on an examination of the blood. When there is a leucocytosis, the predominating cells being lymphoblasts or myeloblasts, the diagnosis is scarcely in doubt. The atypical leukæmias are the ones which cause difficulty. It should be remembered that anæmia and thrombocytopenia are also constant features of the blood picture.

Lymphocytosis may occur in a number of diseases. In glandular fever the lymphocytes may reach a level of 30 to 40 thousand. Though the lymphocytes may form a high proportion of the total, and may be rather atypical in appearance, they are mature forms. Glandular fever cells are present. There is no anæmia. The heterophile antibody content of the serum is high. In cases of doubt repeated blood counts should be done. These will show a gradual fall in the leucocyte count.

In pertussis there is usually some rise in the total leucocyte count towards the end of the catarrhal stage and occasionally the count may exceed 100,000 per c.mm. In such cases the maturity of the lymphocytes should help to exclude leukæmia (Newns and Pearson, 1937).

In young children other acute infections may give rise to a striking leucocytosis with an increase in the proportion of lymphocytes, which are, however, mature in type. The spleen in such cases is often enlarged and in consequence they have frequently been misdiagnosed as leukæmia.

If hæmorrhage is a prominent feature leukæmia may be mistaken for thrombocytopenic purpura (p. 1082). In the leucopenic forms of leukæmia, aplastic anæmia may cause difficulty (p. 1087). In difficult cases it is essential to examine the bone-marrow (*e.g.* by sternal puncture).

Agranulocytosis associated with a severe angina may superficially resemble leukæmia, particularly some of the atypical varieties where there is a leucopenia. Here again atypical white cells should be looked for in the blood and if necessary the bone-marrow should be examined.

In any case of doubt a bone-marrow biopsy should be performed. Since the prognosis is so bad every effort should be made to arrive at a definite diagnosis.

Prognosis. -No cure is known. Treatment, which is designed to relieve symptoms and prolong efficiency, has no material effect in prolonging life. Death in the acute forms of leukæmia usually occurs within six months of the onset of the disease.

Treatment.—The most that can be expected from any form of treatment is a temporary and fleeting remission. Bessis (1949) has reported that exchange transfusion has induced temporary but dramatic clinical and hæmatological improvement in acute leukæmia with a subsidence of glandular and splenic enlargement as well as a reversion of blood and marrow pictures to normal. This result has been confirmed by other workers and in our own experience a comparable result can be obtained with large quantities of fresh blood or fresh plasma. The best effects are obtained in the lymphatic type. Aminopterin has likewise yielded the best results in the acute lymphoblastic leukæmia of childhood. Remissions have also followed treatment of this type of leukæmia with ACTH or cortisone (Dameshek, 1950; Stickney *et al.*, 1950). Farber (1950), considers that the results with ACTH or cortisone are inferior to those obtained with folic acid antagonists (aminopterin and amethopterin). Of seventeen children treated with ACTH five had complete remissions which lasted up to ten weeks. Irradiation is contraindicated and may stimulate the disease.

Thiouracil has been tried in some cases. This reduces the high metabolic rate, abolishes the fever and seems temporarily to make the patient more comfortable. It has no effect on the primary disease and is obviously purely symptomatic in effect.

Chronic myelogenous leukæmia

This form of leukæmia is rare in children and is only met with towards the end of the first decade. The incidence is slightly greater in the male than the female sex.

Clinical features.—The symptoms are insidious in onset, with gradually increasing weakness and lassitude. At the same time gradual enlargement of the abdomen is noticed and this is frequently the symptom that brings the patient to the doctor. Anæmia is not a striking feature in the early stages of the disease and there is usually little disturbance in the child's general health. Examination of the blood at this stage will reveal the typical blood picture. Splenomegaly (as in the adult cases) reaches a considerable degree. The spleen may occupy the greater part of the left side of the abdomen and often reaches below the iliac crest and may cross over the mid-line. The liver is also considerably enlarged and may reach as low as the umbilicus.

There is usually a moderate enlargement of the lymph glands especially in the cervical region. Rarely the lymph nodes of the mediastinum and abdomen become large enough to cause pressure symptoms.

Hæmorrhages may occur late in the disease. They may take the form of skin hæmorrhages—petechial spots or ecchymoses, or there may be hæmorrhages from mucous membranes, *e.g.* mouth, nose, gastro-intestinal and urinary tracts. Occasionally retinal hæmorrhages occur.

Bone pains like those met with in acute leukæmia may occur; they are of similar origin. Pain due to abdominal distension is a common symptom.

The *course* of the disease is rather shorter than in the adult, being two to three years, but there are remissions from time to time during which the symptoms improve and the blood count becomes more normal. Ultimately progressive weakness and asthenia develop and the patient dies of anæmia and exhaustion.

Diagnosis.—This is rarely in question, since an examination of the blood will put the diagnosis beyond any doubt.

Treatment.—As in adults irradiation of the spleen and bone-marrow may produce a temporary regression of symptoms. This may be carried out by means of X-ray irradiation or by radium. Following a course of irradiation the leucocytes diminish in number and the blood picture reverts to normal, though immature cells never completely disappear. The anæmia slowly improves and the spleen decreases in size to a varying extent. A remission lasts usually several months and then the leucocyte count slowly rises. Further courses of irradiation may be given though the effect gradually diminishes.

The best alternative to irradiation is urethane which because of ease of administration (by mouth) and the relative infrequency of unpleasant effects is often preferred. The usual dose is from $\frac{1}{2}$ to 1 gm. three or four times a day with a gradual reduction in frequency of administration when the leucocyte count reaches 50,000 per c.mm. The effects continue after cessation and treatment should be omitted when the count reaches 20,000 per c.mm. Hæmorrhagic symptoms or a low platelet count are contra-indications to treatment with urethane.

Aleukæmic leukæmia (leucopenic leukæmia)

The terminology of this variety of leukæmia is unsatisfactory as it suggests that it is a separate entity. Many cases of acute leukæmia in children pass through an aleukæmic phase, but in a few there is persistent leucopenia throughout the course until the final stages, when a terminal leucocytosis generally occurs. The pathological changes are identical with those of the more typical case, and the symptoms are the same.

Diagnosis is sometimes very difficult and the condition may be confused with aplastic anæmia and agranulocytosis. In leukæmia, however, immature cells can usually be found in the peripheral blood. Where there still remains a doubt a bone-marrow biopsy will clinch the diagnosis.

Chloroma

This is a very rare tumour but its relation to leukæmia warrants a short description. It is a condition in which a leukæmic blood picture is associated with the presence of localized masses, usually greenish in colour, generally connected with periosteum. The common sites for these tumours are the orbit, face, skull and ribs, but they may occur in the internal organs,

especially the liver and kidneys. The tumours are usually grass-green in colour, which fades on exposure to the air.

Microscopically the tumours are composed of non-granular mononuclear cells indistinguishable from the cells of leukæmia and lymphosarcoma.

The patients have the usual clinical symptoms of leukæmia and in addition show the typical swellings of the skull or ribs.

Progressive exophthalmos is a characteristic feature with an intraorbital tumour. Pressure on nerves and other structures may occur.

The blood picture shows typical leukæmic changes. The immature non-granular cells which predominate in the blood are now considered to be immature myeloid cells.

Polycythæmia

Polycythæmia signifies an excess of cells in the blood but in practice this refers only to erythrocytes. In the first place it has to be borne in mind that polycythæmia may be entirely relative due to a temporary concentration of the blood from diarrhœa, vomiting or sweating. Such states of dehydration are common in infancy. Diagnosis is assisted by the fact that all elements of the blood become equally concentrated. Indeed, the state of the blood is a good index of the degree of dehydration.

True polycythæmia, a real excess of erythrocytes, is always associated with increased blood formation and often with an increased blood volume. The polycythæmia may be a primary condition as the result of an unexplained hyperplasia of the erythron accompanied by an increase in blood volume and in the number of capillary vessels. This primary disease, polycythæmia vera (Vaquez-Osler disease), is rare before the third decade. The youngest recorded case is in a child of six (Halbertsma, 1933). In infancy and childhood polycythæmia may be found as a phenomenon secondary to any disease in which there is chronic anoxæmia.

This secondary polycythæmia, usually known as erythrocytosis, is a compensatory reaction whereby the blood is given an increased oxygen-carrying capacity to cope with a state when tissue oxygenation would be imperfectly performed by normal blood. The physiological polycythæmia present at birth (p. 1046) is attributed to the anoxæmic condition of intrauterine life.

Chronic polycythæmia of cardiac and pulmonary origin is most marked in congenital abnormalities of the heart, *e.g.* pulmonary stenosis, Fallot's tetralogy in which red cell counts of 8 to 10 million per c.mm. are quite common. Milder degrees are found in emphysema, pulmonary fibrosis, chronic heart disease and Ayerza's disease. Drugs such as the aniline derivatives which give rise to sulphæmoglobinæmia and methæmoglobinæmia often cause polycythæmia as well. Polycythæmia is also found fairly constantly with Cushing's syndrome as well as in diseases such as Huntington's chorea, which affect the diencephalon.

DISEASES ASSOCIATED WITH SPLENOMEGALY

Although the exact functions of the spleen are only imperfectly understood, it is generally agreed that the organ contains more reticulo-endothelial tissue than any other site in the body, that it undoubtedly plays some part in the formation of antibodies, that it conserves iron derived from broken down corpuscles and that it acts as a reservoir for blood until it is required in another part of the body.

Splenomegaly is a frequent and important sign of disease in children. The causes are diverse; the interpretation often difficult. On general principles the spleen may be enlarged by reason of congestion or hyperplasia; this last may be hyperplasia from increase in the normal functions of the organ or from a malignant process.

Consequently, the spleen is found to be enlarged in most infective conditions, bacterial, spirochætal or protozoan, by reason of phagocytic activity and antibody formation. Enlargement also occurs with increased pigment metabolism, as with many anæmias, especially those of hæmolytic type, with lipoid metabolic diseases, with malignant hyperplasia as in leukæmia and from portal congestion as with heart failure or cirrhosis of the liver. Many of these conditions have already been described. There remain a few, which are not splenic diseases, but are diseases in which splenomegaly is prominent and in which there are associated blood changes.

Splenic anæmia (Banti's syndrome)

This chronic disease is manifested by enlargement of the spleen, a progressive anæmia with leucopenia, a tendency to gastric hæmorrhage and, in the later stages, cirrhosis of the liver and ascites.

The ætiology is obscure and it is quite certain that Banti's syndrome may arise from a number of causes. Most commonly the syndrome appears to have a hepatic origin so that the splenomegaly is caused by venous congestion directly related to the end result of an inflammatory process in the liver. In principle, any condition leading to a rise in portal pressure followed by fibrosis in the liver and spleen is liable to give rise to the syndrome.

The disease is rare before puberty. Martin (1936) reported two cases in children.

Pathology.—The spleen is firm and large with a thickened capsule often adherent to the diaphragm or other surrounding structures. Microscopically the spleen shows fibrosis with dilatation of the sinuses. Periarterial hæmorrhages are commonly found in the spleen; these may become fibrosed and impregnated with amorphous iron pigment (Gandy-Gamna nodules). The spleen and portal veins often show atheromatous thickening. In advanced cases the liver is the site of portal cirrhosis. Œsophageal varices are common.

The cause of the anæmia, apart from direct blood loss, is obscure. The anæmia is hypochromic and progressive; the leucocyte count is frankly neutropenic.

Course.—Three stages are recognized. There is first enlargement of the spleen with a slowly developing anæmia lasting for some years. Next a short transition stage of some months during which the liver becomes enlarged and jaundice often occurs. In the terminal stage there is advanced cirrhosis of the liver, ascites, cachexia and hæmorrhages.

Gastric hæmorrhage occurs in about 50 per cent. of cases, whilst intramuscular bleeding, purpura and epistaxis are sometimes found.

Diagnosis.—All other possible causes of splenomegaly should be eliminated before accepting a diagnosis of splenic anæmia.

Treatment.—Each individual case requires careful judgment. In some the disease is mild, chronic and of long duration uncomplicated by hæmorrhage. In such, simple medical treatment with large doses of iron are helpful, whilst X-rays may be applied to the spleen in order to reduce the size, but this has the disadvantage of rendering any future operation more difficult on account of adhesions. Most authorities agree that splenectomy is of definite value especially when the organ is enlarged by reason of splenic vein thrombosis or when recurrent hæmorrhages appear to be brought about by splenic vein congestion. Splenectomy is, however, usually combined with one of the forms of venous anastomosis, more particularly lieno-renal juncture. Venous anastomosis offers most chance of relief or cure, but the operation, like all other treatment, should be undertaken before the onset of advanced cirrhosis and ascites.

DISEASES OF THE LYMPHATIC SYSTEM

The lymph glands into which the lymphatics drain are widely scattered throughout the body and serve as filters of the lymph, bacteria and other foreign particles being removed. The lymph glands also have the function of producing new lymphocytes. During the early part of childhood the lymphatic tissue undergoes a remarkable hyperplasia in response to infection. This lymph gland enlargement may persist for some considerable time after the subsidence of an infection. The lymphatic tissue in the nasopharynx, the tonsils and adenoids, and the cervical glands draining them, and the mesenteric glands are particularly liable to become enlarged. As the child grows older the lymphatic tissue undergoes retrograde changes and the tendency to lymphatic hyperplasia diminishes in late childhood.

Diseases of the lymph vessels

The thoracic duct.—Obstruction of the thoracic duct is extremely rare in children. It is occasionally caused by pressure from tumours, generally lymphosarcomata. Chylous ascites results, the fluid being milky in appearance, containing a considerable proportion of fat, sometimes as high as 5 per cent. The amount of fluid is large and tends to recur when removed by paracentesis. Very rarely chylous ascites may be due to a wound of the thoracic duct.

Lymphangitis.—This is an inflammation of the lymphatic vessels and may be acute or chronic.

ACUTE LYMPHANGITIS.—This occurs when there is relatively little local reaction to infection, which rapidly travels up the lymphatics to the regional lymph nodes. The superficial lymph vessels may be seen as red lines. A diffuse cellulitis, however, may obscure this characteristic appearance.

Treatment should be directed to the site of infection by the employment of appropriate chemotherapeutic drugs, which will rapidly clear up the infection.

CHRONIC LYMPHANGITIS.—This is best seen in the primary tuberculous complex of the lung or abdomen. Infiltration of the regional lymphatics of lung and mesentery with caseous material can be demonstrated in post-mortem specimens.

Tumours of the lymphatics.—Lymphangiomata are raised cystic tumours which may occur in various sites, in the limbs or on the trunk, neck and elsewhere. It is one of the causes of macroglossia. The tumours are soft and rather indefinite in outline. The overlying skin may be normal or it may be the site of a hæmangioma. They do not tend to get any bigger. The tumours are insensitive to irradiation. Surgical removal is the best treatment, though the tumours may recur.

CYSTIC HYGROMA is a form of lymphangioma occurring in the neck and containing large cystic spaces lined with endothelium filled with clear or straw-coloured fluid. They frequently cause pressure symptoms. Surgical removal though difficult is the only effective treatment.

Diseases of lymph glands

The chief causes of enlargement of lymph glands are listed as follows:—

(1) Simple inflammation, acute and chronic. Infection of lymph glands from a neighbouring focus, *e.g.* the cervical glands in acute tonsillitis. The common infecting organisms are streptococci and staphylococci.
(2) Tuberculosis. Most often an affection of regional lymph glands, chiefly in the cervical region. On rare occasions a generalized tuberculous adenitis occurs.
(3) Glandular fever.
(4) Hodgkin's disease.
(5) Leukæmia.
(6) Syphilis. This is nowadays a rare cause.
(7) Primary malignant tumours, *e.g.* lymphosarcoma.
(8) Secondary malignant tumours.
(9) Some specific fevers, *e.g.* rubella, measles.

Acute lymphadenitis.—An acute inflammation of lymph glands secondary to an infection of neighbouring tissues. For example, infection of the scalp may cause enlargement of the occipital group of glands. The cervical glands are commonly infected from the tonsils. The mediastinal glands are enlarged in pneumonia and the mesenteric glands in typhoid fever. In children inguinal adenitis is often due to septic skin lesions of the lower extremities. Bacterial toxins as in diphtheria may also be a cause of lymphadenitis.

Symptoms.—These vary according to the severity of the primary infection. The affected glands enlarge and become painful, and are tender to the touch. The overlying skin may be reddened. There is often a considerable degree of peri-adenitis and the glands become matted together to form a brawny mass. There may be protective spasm of neighbouring muscles as in the neck when the head is pulled over to the affected side.

Constitutional symptoms vary with the severity of the infection. There is usually in the first two or three days some fever and a feeling of malaise.

The glands may resolve after a varying period ; they remain enlarged for some weeks, or may suppurate either within a few days of the onset or after an interval during which the gland remains hard and brawny. If sulphonamide or penicillin therapy is given early the inflamed lymph glands usually subside rapidly and suppuration is prevented.

Suppuration fortunately is rare in mediastinal adenitis, as it may lead to a fatal mediastinitis. The glands may, however, enlarge sufficiently to cause pressure symptoms, *e.g.* brassy cough, stridor or dyspnœa.

Treatment.—Treatment of the primary focus of infection by chemotherapeutic drugs brings about a rapid subsidence of the lymphadenitis, if started early enough. The affected parts should be kept, as far as possible, at rest. If the glands are painful heat may be applied in the form of poultices or from an infra-red lamp. When suppuration occurs with abscess formation the gland should be incised.

Chronic lymphadenitis.—This is the result of recurrent or persistent infection in the area from which the gland receives its lymphatics, *e.g.* chronic enlargement of the tonsillar glands in recurrent tonsillitis ; or of the occipital glands in infantile eczema of the scalp, in which the lesions have become secondarily infected. Chronic lymphadenitis may also be due to tuberculosis, glandular fever, syphilis, brucellosis, Hodgkin's disease, lymphosarcoma and leukæmia.

Diagnosis may only be possible after careful histological examination of a gland obtained by biopsy.

Treatment of simple chronic lymphadenitis should be directed to improving the general health. Heliotherapy is valuable. The glands subside gradually if the primary source of infection is dealt with, *e.g.* tonsillectomy in the case of chronic enlargement of the tonsillar glands.

Tuberculous adenitis.—Tuberculosis of the mediastinal and mesenteric glands is dealt with in the section on tuberculosis in ch. XIX. Tuberculous cervical adenitis is still a relatively common disease, though much less frequent than formerly. There was an increase in its incidence during the war owing to the dispersal of the child population into country districts where much unboiled milk infected with tubercle bacilli was drunk. The infection may also be of the human type. Tuberculosis of the axillary or inguinal group of glands is rare. It is sometimes secondary to a tuberculous skin lesion. In the case of cervical adenitis the primary focus is usually in the tonsils, the lesion in conjunction with the secondarily involved cervical adenitis constituting a primary complex. The cervical

glands enlarge to a varying degree. At first one side is affected but the other side is soon involved. One or more glands may be enlarged; for a time they are discrete and mobile. Later they become matted together. They are painless from the first. As the disease progresses the glands become adherent to adjacent structures and to the skin, which becomes discoloured. Finally the caseating gland ruptures through the skin discharging its contents. A persistent sinus is common. During the active phase of the adenitis there is some affection of the general health with malaise, anorexia and loss of weight.

In many cases, however, the glands slowly resolve. Calcification takes place which can be detected by X-ray. Glands which are apparently healing may suddenly flare up as a result of a secondary infection with pyogenic organisms, and may break down. Fortunately hæmatogenous spread from cervical adenitis rarely occurs. Healing eventually takes place even in untreated cases though there may be ugly scar formation.

Diagnosis.—Tuberculous cervical adenitis may be extremely difficult to diagnose. It must be distinguished from simple chronic adenitis, Hodgkin's disease, and lymphosarcoma. A negative 1 in 100 Mantoux test rules out tuberculosis as a cause of the adenitis, but a positive one may be indicative only of an earlier primary lung infection. Often a diagnosis can only be arrived at by observing the course of the infection. If caseation occurs the adenitis is certainly tuberculous. The bacilli may be isolated from the caseous discharge, or definite tuberculous lesions found in an excised lymph gland.

Treatment.—Conservative treatment is practised whenever possible. This consists of general hygienic and dietetic measures. Rest to the neck by splintage and heliotherapy or actinotherapy are valuable. The tonsils should be removed at the outset.

Excision or expression of the lymph gland through its capsule may be carried out if caseation occurs. When the gland capsule has been broken through this is not practicable. Local curettage of the gland is practised by some surgeons, whereas in more extensive cases complete excision of the affected glands may be necessary.

Lymphosarcoma.—This malignant growth is rare in children. It may arise from superficial lymph glands or from internal glands such as those of the mediastinum or abdomen. Metastases take place widely especially in the lungs. The spleen is often involved. The affected glands enlarge rapidly and may cause pressure symptoms especially in chest or abdomen where the superior or inferior cava may be obstructed. In the early stages the glands in the neck may resemble those of Hodgkin's disease, but the capsule tends to rupture and local invasion occurs. Histologically lymphosarcoma differs from Hodgkin's disease in the uniformity of the cell type. There is no increase of reticulin. The mature lymphocytes are replaced by large hyperchromatic cells with a small amount of cytoplasm and a round or oval nucleus.

The blood may show a secondary anæmia. In some cases the blood picture is identical with that of lymphatic leukæmia and it may be extremely difficult to differentiate between the two diseases. There appears

in fact to be a close relationship between them. The histology of the glands may be identical in both conditions.

Lymphosarcoma is very radio-sensitive and responds rapidly to radiotherapy. The effect is a transient one, however, and the glands soon enlarge again as soon as radiation is stopped. The disease is uniformly fatal.

Lymphadenoma (Hodgkin's disease).—An invariably fatal disease characterized by painless enlargement of the lymphatic glands, resulting in progressive anæmia and cachexia. Males are affected more commonly than females. The disease is uncommon in children. There is no hereditary or familial incidence.

Ætiology.—The causation is unknown. The old view that the disease was a variant of tuberculosis has now been discarded. The latter affection, however, is frequently a complication. The most widely held view is that Hodgkin's disease is an infectious granuloma. The histological picture is that of a granuloma. The ætiological agent is not known though it may be a filterable virus.

Many pathologists consider, however, that Hodgkin's disease is a neoplasm, a form of lymphoblastoma, which may develop into lymphosarcoma on the one hand, and into lymphatic leukæmia on the other.

A third view is that the disease, like mycosis fungoides, occupies an intermediate position between the infectious granulomata and the neoplasms.

Pathology.—The organs principally affected are the lymph glands, spleen, liver and bone-marrow. The lymph glands become enlarged, the cervical glands being as a rule the first affected. The disease may spread to the mediastinal and abdominal glands. The spleen is enlarged and is usually infiltrated, discrete irregular masses of Hodgkin tissue giving the typical "hardbake" appearance. The liver also becomes infiltrated. The cut surface shows irregular masses of Hodgkin tissue, chiefly in the portal areas. Nodular and diffuse infiltrations of the bone-marrow occur, which are probably the cause of the severe anæmia of the later stages. There may be infiltrations in the spinal canal. Lesions in the lung are relatively common. There is a diffuse infiltration along the bronchi, involving the lymphatic tissue in this situation. Occasionally there is consolidation of a whole lobe giving the appearance of pneumonia.

The histological appearances are the same in all the organs but are most characteristic in the lymphatic glands. There is a proliferation of the lymphoid cells followed by the appearance of large pale cells with elongated vesicular nuclei. Soon the normal architecture of the glands is destroyed. Dorothy Reed giant cells are scattered throughout the gland and there are usually many eosinophils.

In the later stages areas of necrosis appear. There is a progressive increase of fibrous tissue and the gland becomes much less cellular. Finally all that is left is a dense mass of fibrous tissue, in which there are new pockets of cells.

Clinical features.—The onset is insidious, the first symptom being a painless swelling of one of the superficial groups of lymph glands, most commonly the cervical. The disease is at first unilateral but later may

spread to the other side. The glands are firm and discrete and can be moved about easily. Later they may become matted together. After the disease has been in progress for some time other groups of glands may enlarge. Evidence of enlargement of mediastinal or abdominal glands may appear, namely pressure symptoms of various kinds. Pleural effusion may occur in intrathoracic lymphadenoma. In most cases the spleen is palpable, but the liver is enlarged in only about a third of cases.

Pressure on the spinal cord may give rise to paraplegia. Sometimes the symptoms resemble those of acute transverse myelitis. Skin manifestations are seen in about one-third of the cases. There may be pigmentation; lymphadenomatous nodules may appear in the skin. Constitutional symptoms are not marked in the early stages but later there is progressive anæmia with cachexia. Fever of an irregular type is common, but occasionally the classical Pel-Ebstein type of fever chart, with periodic bouts of fever alternating with apyrexial phases, is seen.

The course is generally prolonged though an acute form of the disease is occasionally met with and is said to be commoner in children than adults. The average duration is eighteen months to three years. No case has ever recovered.

Hæmatology.—The blood changes are neither characteristic nor diagnostic but a blood count must be performed in order to exclude leukæmia or other conditions in which splenomegaly and glandular enlargement are presenting signs. The anæmia is usually progressive and of hypochromic type but is not severe until the terminal stages. Occasionally the anæmia may be leuco-erythroblastic. In these circumstances, the bone-marrow is affected by the primary disease. The leucocyte count is very variable and the number of leucocytes bears no relation to the severity or the stage of the disease except that in the terminal stages the count is usually leucopenic. Only about 15 per cent. of cases show the eosinophilia so frequently stressed as a diagnostic point. The blood platelets are usually plentiful but may be reduced in the terminal stages.

Diagnosis.—This may be difficult in the early stages. Biopsy of the gland is essential. The histological picture is usually distinctive though occasionally the hyperplastic type of tuberculosis may cause difficulty. The endotheloid cells and Dorothy Reed cells will enable lymphadenoma to be distinguished from lymphosarcoma and aleukæmic leukæmia.

Treatment.—The affected glands should be irradiated with X-rays or radium. This produces a temporary remission though the glands later enlarge again. Further courses of irradiation should then be given. The blood should be carefully watched during treatment as the irradiation may give rise to a severe anæmia. Surgical extirpation is useless. Arsenic, at one time much used, is of no value. Nitrogen mustard treatment has given good results especially in generalized cases, and when viscera are involved as well as in cases insensitive to irradiation (Videbaek, 1949).

Status thymo-lymphaticus.—Modern opinion is extremely sceptical of the existence of this condition, which Paltauf, in 1889, described and claimed to be a common cause of sudden death. There was a generalized enlargement of lymphatic tissue throughout the body with splenomegaly

and enlargement of the thymus. Death was said to be cardiac in origin. Hammar and Boyd (1932,1936) have shown that a considerably enlarged thymus is physiological in children who often exhibit general hypertrophy of the lymphatic tissue. Young and Turnbull (1931) came to the conclusion that there was no evidence that status thymo-lymphaticus existed as a morphological entity. Certain children do seem to have a low resistance to anæsthetics, vaccine and serum injections, but there is no evidence that this is due to hypertrophy of lymphatic tissue. More accurate autopsies reveal the cause of many hitherto unexplained deaths though there are still cases in which no definite cause of death can be found (see also p. 704).

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CHAPTER XXV

FUNCTIONAL DISORDERS OF THE NERVOUS SYSTEM

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1. *INTRODUCTION*

AN attempt to picture the nervous disorders of childhood must abandon the idea of drawing a hard and fast line between what can be called normal and abnormal. The child is at one and the same time sensitive and helpless, aggressive and destructive. His physical well-being is subject to a number of stresses, yet, like a small boat, he has a strong tendency to right himself. The same is equally true of his nervous balance, and symptoms and regressions which would appear sinister in an adolescent can be handled with understanding and confidence that the outcome will be but a further step on in growth.

In studying children it is often difficult to decide at what stage and from what source an unhealthy stress arises. Children who remain undisturbed by the worst air raid can be profoundly affected by an emotional storm between their parents, and it is impossible to study the child without at the same time including in the picture the child's parents and his environment, which so profoundly modify both the rate and the main directions of his development.

Then again, it is not always easy to say at what point these influences begin to bear. A good deal is written on the psychology of pregnancy and pre-natal influences, but it has to be admitted that many timid and inexperienced mothers bear perfectly normal children and there is much to suggest that shocks during pregnancy have little effect on the child, although they may deeply influence the subsequent development of the relationship between the mother and her child. Quite the reverse is true of physical injury, and from recent work it would appear that the rôle of minimal physical trauma during pregnancy or during labour has in the past been underestimated as a cause of obscure congenital defects of one kind or another. Very debatable ground too is reached by the eugenists, and in discussing the rôle of inherited nervous instability it is to be remembered that everybody, including the parents themselves, will expect the child of nervous parents to be himself nervous.

It is a common fallacy to regard the infant and growing child as a kind of soft receptive medium, moulded entirely by parents and others who have charge of it. It is important from the beginning to recognize the dynamics of such a relationship. Whilst it may be true that the influence of his mother will have an important bearing on everything he does, and will certainly leave a lasting impress on his behaviour pattern throughout life, it is only necessary to observe the different children in one family to realize that each child has its own way of dealing with that

impact, and that the child's individual growth and development has a personal quality from the start. It is therefore profoundly true that while the resilient quality of a child's resistance to trauma may lead to battle, it is also the very life stuff of his virility and independence, not to be purged out of him and dismissed as original sin.

It is nearer the truth to look on the influence of the mother on the child as a relationship which is from both sides a growing and developing force, influencing both, changing and shifting, the general tendency on the part of the parent being to cherish and protect, and on the child's side a fluctuation towards finding comfort in that shelter and an opposite urge to repudiate its need for care and to seek new sensation and adventure. Just as the parent will often feel guilty at her " neglect " of the child, which may be the way her mind interprets something which goes wrong with him, so the child may feel guilty (and profoundly discouraged) when one of his more outgoing experiments ends in disaster. As most occasions on which a doctor is called to see a child are regarded by somebody as a disaster, it is important that he at least should be aware of the possibility of this tide of anxiety setting in, should be able to recognize some of its sources, and thereby be able to counter its effects.

Bearing in mind the very strong trend towards normality, he will often confine his efforts to being a buffer and an ameliorative factor, so that both sides may win the battle with honour and no love lost!

It is only when these occasions of alarm or frustration result in a loss of love that a truly anxious and guilt-ridden attitude will impair this relationship and lay the foundation for a lasting " nervous " state, which in itself may be an attempt to adjust, as indeed all neurosis is.

It will not be found possible to describe and understand the nervous disorders of childhood without some picture of the underlying dynamics with which the situation is so often highly charged. Any picture drawn in terms of environment alone will seem incomplete and unconvincing, so that, without embarking on theoretical and debatable mechanisms, an attempt will be made to describe the common disturbances seen in childhood, and to see them in relation to the stuff of which the child is made, his physical health, his temperamental stability, his parental background, the home in which he lives and the ordinary things which he is expected to learn to do.

Many more people than formerly are to-day engaged in some form of child study, in crèches and nursery schools, in child guidance clinics, and in training schools for those who are to come in contact with children. In spite of all this, mothers will continue to be anxious about children who are not doing well, and will continue to look to the family doctor as their first and greatest hope in gaining advice. The physician's ability to recognize nervous mechanisms in common disorders shown by children will enable him to approach these abstract problems with greater confidence in his own judgment. Without this, he will find himself frequently baffled by a trivial symptom which persists only because it serves a dynamic purpose in dealing with what is essentially an inner and personal

situation. Granted this understanding, the doctor, more than anyone else, will have the first chance at helping to reach an adjustment and thus restore confidence to both sides.

2. NORMAL DEVELOPMENT

The clinical recognition of an abnormality can only be reached from a clear conception of the limits of normal development. It is now recognized that the range of normal development is very wide and the factors governing differences within the range are very varied. Nor is the rate of development constant, in so far as a child may be quick in walking and late in talking, or may develop in every way rapidly until an intercurrent illness occurs, not in itself very serious, but which may retard the whole process, or even go so far as to produce a clinical picture suggestive of deterioration.

In the last twenty years a number of studies have been made, based on careful observation of children from day to day. Thus gradually a factual picture has been built up, especially by Gesell, who, with a special technique of continuous observation and recording, succeeded in giving a detailed cross-section of the infant's capabilities, from the first weeks of life onwards.

Such rough and ready scales as " walking by one year and talking by two " must give place to a conception of development in terms both of heredity and environment, of general scales and individual variations out of which a scheme has been perfected. Thus, according to Gesell, in the first quarter of the first year the infant gains control over the muscles which moves his eyes. In the second quarter (16 to 28 weeks) he is able to command the muscles which support his head and to move his arms. He reaches out for objects. In the third quarter (28 to 40 weeks) he gains command of his trunk muscles and is able to sit. He can use his hands in grasping, manipulating and transferring objects. In the fourth quarter (40 to 52 weeks) he extends command to his legs and feet; to his forefinger and thumb. He can stand upright and can use his hands in poking and plucking movements. In the second year he learns to walk and run. He can articulate words and phrases; he acquires some control over his bladder and bowels; and he attains a rudimentary sense of personal identity and of personal possession. In the third year he can use sentences, using words to express his thoughts. He begins to understand his environment and to comply with cultural demands. In the fourth year he asks innumerable questions, perceives analogies and displays a tendency to conceptualize and to generalize. He is nearly self-dependent in his home routine. At five his motor control is well matured. He can hop and skip. He talks without infantile articulation and can narrate a long tale. He prefers association play and feels a socialized pride in his clothes and accomplishments.

This scale is of particular value in adoption cases, when it is important to establish at an early age that normal potentiality for development exists. Using the Gesell scale in the hands of skilled and experienced

testers, it is possible to establish with a fair degree of certainty whether a child is or is not mentally defective, from about the age of three months.

No scale of development can be said to have universal validity, and delayed development of one capability alongside others which are average cannot be taken as having any certain prognostic significance. When retardation occurs all along the developmental line and every skill is acquired late and with difficulty, then the picture has in it much to suggest mental defect.

Judging very broadly, an infant's development can be measured by his " milestones," the ages at which he learns to grasp, to hold, to stand and to walk, by his alertness in responding to visual and auditory stimuli, and his social response to people, his stability and capacity to appreciate new circumstances and to adapt to changes, and later his verbal development both in learning and using sounds and then words and his response to speech.

Certain nervous difficulties can affect his development in these directions, so that a misleading impression of mental defect is created, and it is as important to recognize this pseudo-arrest or retardation of development as it is to know the significance of these changes when they occur and exist outside environmental causes. The younger the child and the more recently his ability has been acquired, the more likely it is that an external event will leave a temporary mark on the tide of his development.

(*a*) *Intercurrent illness*, especially when it involves confining an active child to bed, will appear to undo in a few weeks the work of many months of acquired habit. During and after an illness it is common to find a child wet at night, or even doubly incontinent and unable to sleep alone or without a light, and by day unwilling to feed himself. This appears to be a result of the combined effects of a period of close nursing attention, and of the unrest and malaise which inevitably accompany sickness. If the child has been in hospital he may have become accustomed to unusual surroundings and constant companionship, with less individual attention than his normal share in a small family. Such situations often lead to a charge of " neglect " by the parent against the hospital. It cannot be too strongly emphasized that the deprivation, often a necessary one, of the individual mother's care may precipitate a withdrawal into a non-progressing state of self absorption. The younger the child (excluding infants), the more likely he is to be affected in this way, and the most striking features are his apathy, which has a positive quality, his refusal to talk, to feed, or to co-operate in any way. Such children stand about and look dazed. If a toy is put into their hands, they will let it fall, or will draw back as if they resented the approach. They appear to have no social contact with the group and it is a long time before they make any. They have great difficulty in mixing and usually they come round by the effort of one individual. Getting them to eat is not easy and they may be inertly incontinent, as if they neither noticed nor cared. Such reactions have been commonly seen in nursery school evacuees, and in children in hospital. The reaction is almost like

that of an adult depression (Spitz), and the effect is like a hibernation from which the child emerges gradually, taking days or even weeks to return to his former state of activity. As such reactions tend to occur in small children it is often impossible to get any clue as to what is going on in the child's mind. The harm done to young children by early separation from their mothers is now clearly recognized. Some children fail to return to a normal child-parent relationship, becoming aloof and lacking in a capacity to form attachments, leading to delinquency and other behaviour disorders (Bowlby, 1951).

Such a condition must not be confused with the genuine deterioration, described in a later section, which follows on some febrile illness which must be presumed to have had an encephalitic accompaniment.

(*b*) *Shock*, due to an accident or an alarming occurrence, may have much the same effect. Here the child is usually disturbed more by the effect of the incident on adults than by the fear engendered in himself. Such a condition may be seen typically in an air raid or an accident which temporarily deprives the child of his normal surroundings, and of the people who normally care for him. Whilst some children appear able to maintain their equilibrium in such circumstances, others react quite severely, going off their food and sleep, and regressing in their habit achievements. When such a reaction has occurred it is important to give the child the maximum of individual attention possible, and not suppose that contact with a crowd of unfamiliar children will work a miracle. Sudden change of environment from family life to a hostel, and some of the results of evacuation, bear a very close resemblance to this regression, which is perhaps most typically seen at the pre-school age of two to five years.

(*c*) *Deprivation.* Similar reactions, in some cases closely resembling a melancholic stupor, may follow the loss of a parent or a much beloved sibling. Here again the situation may be made worse by the accompaniments of grief, so that the child's reaction passes unnoticed during the actual crisis. These states of withdrawal should never be treated by a mere change of surroundings. To send a child away to an unknown relative or to a convalescent home may apparently restore normality, but such removals should only be carried out if and when necessary, and throughout safeguarding for the child as much individual attention as reasonably possible. It is better that attention should be directed to the child's emotional need of love and reassurance. Handling will need to be firm and a compensating interest should be sought. The individual attention should be the reverse of " spoiling " since its aim is to foster even more independence than was necessary before. Fortitude is a quality as desirable in the child as in the adult.

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3. *MANAGEMENT AND EARLY TRAINING*

Now that so much of the emphasis on early childhood difficulties comes from a psychological angle, there is a dangerous tendency to suggest that the mental happiness of the individual is ensured for life, or banished for ever, by the way he is handled during his first months. Returning to the conception of early infancy as a shifting mosaic which later consolidates into well-marked behaviour patterns or trends, it is true to say that many of these trends will follow on events which take place at a very early age. Thus, a disturbed infancy, with a restless crying child unadapted to its food and feeding training, will leave its mark both on the child and its parents.

It is therefore worth while investigating such a maladjustment in order to discover what are the forces which tend to maintain it. The desire to feed and the desire to be fed are both there, and the means to achieve satisfaction are provided by Nature, and it requires more than mere wilfulness to prevent their working smoothly into a régime. In the natural desire to establish breast feeding without any fuss, perhaps too little attention is paid to the need for patience on the part of the mother and nurse, for none will be shown by the hungry infant. This aspect is well brought out by Middlemore (1941). Her classification of infants who are difficult at the breast deserves a wider study. Her observations show how frequently an infant takes time to acquire the necessary skill and vigour to get what he needs from the breast from which he has to feed.

Middlemore draws a distinction between the lazy " inert " sucker, and the restless impatient child who gives up after a too vigorous onslaught, and she succeeds in describing most vividly the usual background to a feeding problem. As in most aspects of children's medicine, " warm hands and a cool approach " work wonders. In establishing a difficult breast feeding, sufficient time must be allowed to both mother and child to learn each other's ways. Adequate recognition must be granted to the anxiety, caused by physical frustration and hunger in the child, and in the mother by her sense of failure to meet her child's needs, probably for the first time. Such anxiety quickly leads to a need for immediate relief, and many mothers who are said to be unwilling to breast feed their children, could more accurately be described as unable to bear the reproach of not feeding them. The reproach in this sense is applied by

themselves at a biological level deeper than consciousness, and the resulting rod is steeped in the brine of anxious relatives' inquiries and condolences.

The quickest, but a most undesirable way out of the dilemma, is a supplementary feed. The infant, having got what it wants easily from a bottle, will not readily persevere with the more niggardly breast, which then tends to secrete less, due to lack of stimulation.

The question may be raised as to why breast-feeding difficulties should be considered at such length in a section devoted to nervous disorders in childhood. The justification is two-fold. First comes the consideration as to whether " nervous " children as a group are more difficult to feed. It is here important to define " nervous " rather more narrowly. Such terms as sensitive, and highly-strung, are often rather indiscriminately applied to children who may be said in general to be over-responsive to stimuli. This tendency is often a source of pleasure and interest to parents, as an assurance to them that their child " notices " and is not without intelligence. His vivid response at first tends to flatter them. They may, imperceptibly to themselves, augment the child's tendency to respond by an unconscious over-stimulation, until eventually the infant can only be reassured that his parents are there, taking care of him, when they actually declare themselves in some way. This in turn becomes the basis for " demanding attention," a phrase which is often used as a mild rebuke in discussing infant management.

In the light of an explanation which takes full cognizance of the infant's need for reassurance, it is seen to have a passive rather than an active quality. In other words, a child is gradually made dependent on a more and more open declaration of his parents' attention. His need for reassurance is real and factual : the point at which it can be met and satisfied will depend very largely on stimulation. This may partly explain the frequently observed elder child's sensitiveness, for it is almost certain that the first child in a family comes in for more attention than those who succeed it.

A second reason for giving careful attention to the psychological aspect of breast feeding is that it is the first and most intimate of all personal relationships. It is intimate in the sense of being a gratification of a biological need of one individual given by another individual by physical means. This is not stating more than the elemental facts of the situation, and they are not altered by being capable of translation into terms of a bottle and a nannie. In either case the instinctive not-to-be-resisted urge to nutritional satisfaction is met by a response which is adequate or not so, steadily met or spasmodically met, surrounded by an aura of peace and comfort, or by an atmosphere of strain and tension. A pattern of behaviour, arising from which will be a series of responses to satisfaction or frustration, will tend to persist and to colour many adult responses of an entirely different content.

Food fads.—Later feeding difficulties do not invariably link with earlier ones. Symptoms may range from the unwillingness of the child to eat, to a series of food fads and phobias. The healthy child will be

receiving varied diet and will be feeding himself with most of it by the time he is eighteen months old. Weaning from breast to teaspoon and from teaspoon to cup is usually not a great difficulty, provided it is undertaken gradually and with patience in the early stages. Harm is done when too high a standard is demanded and the small child scolded for messes and mishaps. If anxiety is shown by parents or nurse over the amount the child takes, the result is often a negativistic refusal on the part of the child to being fed. When much concern is shown as to the kind of food he takes, and undue care taken with specially prepared dishes, the result is more often an apathetic lack of interest in any food at all. In either case, the child's reaction can be understood if it is regarded as a defensive repudiation of the burden of responsibility imposed by his mother's concentration of interest, either in his getting food, or in the food he gets, which is not quite the same thing. Relief is obtained by deflecting the excessive interest to a more positive kind of achievement, such as walking or climbing, and by readjusting the attitude between the mother and child, which alone could make such a concentration of interest possible.

The specific food fads tend to come later in the chronological progress. Quite often the starting point of such a situation is an actual gastric upset of some kind and the dislike of a particular food may relate to the memory of being sick after eating it. More often the food will have some disturbing association in the child's mind. Certainly very frequent dislikes suggest that the association may be with some other physical secretion. Children so frequently dislike milk, red meat, white of egg (like mucus), porridge (like vomit), spinach (like fæces), that it is difficult to avoid the conclusion that the association in their minds is to some bodily function, or one of the excretory processes.

Negativism.—The whole clinical picture of feeding difficulties is often linked with that of *negativism*, so commonly shown in the child of pre-school age, broadly speaking from two to four years old. It is quite true that at this stage many of his defences are made in terms of refusal. This refusal in some children becomes almost a habit, and every suggestion or direction is countered by him. As shown above, the refusal to take food may be a rejection of the breast, a refusal to be weaned, a general refusal of food later on, or of particular foods, or it may widen into a lack of appetite, both for taking food and other activities suggested for him.

In the normal confident child, some negativism is common, but it is easily overcome by tact and a little care in making the first approach to a project. When it becomes a serious problem, serious in the sense that the mother feels herself unable to cope with it, the picture has to be seen as carrying a positive quality, and as having a value for the child which is much more than the strategic gain of having defied his mother.

Most commonly the situation will be one in which the mother has shown undue anxiety over the performance of some normal activity. It then becomes, for the child in turn, a weighty situation as to whether he succeeds in meeting her wishes. The stakes are doubled and it is no

longer easy for the child to tolerate his own dangerous imperfections. On the other hand, a child may be unusually adventurous and his negativism is aroused by being denied some particular outlet. A temper outburst may follow, or a generalized refusal to co-operate in any form of activity suggested. Far from enjoying his outburst the child will often appear somewhat distressed to find himself taking the wrong side, as it were. No longer in line with the powers that reign, he has to augment his simple refusal with violence and aggression, hating, biting, kicking, and defying the very alarming realization borne in on him that sooner or later this will have to stop. As a rule the outburst reaches a final fling and a storm of tears, after which some children appear quite exhausted and pallid, unable to eat and often much relieved by treatment with glucose. Such children may be the products of a large and otherwise happy family, well brought up, but with a tendency to jealousy or insecurity in relationships within the family.

Thus, common causes of the so-called temper tantrum are the denial of a normal outlet by restrictive severity or lack of imagination in the parents; secondly, the over-weighting of a situation by the parents' own anxiety which makes success or failure too important and thus a source of anxiety in the child; or thirdly, the presence of a sense of rivalry within the family constellation.

Jealousy situations.—Family relationships undergo a progressive development and elaboration parallel with the physical and mental development of the child. Just as his first physical need is concerned with nutrition, so his first personal relationship is with his mother who provides it for him. As his sphere enlarges, it must include his father and his siblings, and a recognition of life and activity going on in the family in some of which he is not expected to participate. Here again, the burden of this is more keenly felt by the first child. Of all the family, he is the one to have been, for a time, an " only " child. He may arrive at a time when his parents are very closely drawn to one another. If he is other than a model child, his presence will tend to interfere with, or actually disrupt, this pull, so that the father may be jealous of the mother's time given to the child, or the mother may resent her child's interference with her enjoyment of her husband's company.

Such an explanation is usually angrily repudiated by the parents, who bring to the medical practitioner problems of management in which these tensions are very evident. The effect on the child, however, is often to create a vicious circle.

When the mother is openly hostile to the child, who for instance cries at night, she will increase both his anger and his fear of being left alone. If, on the other hand, she cannot admit to the hostility which then has to be suppressed, she will feel a sense of guilt arising from her fear of being hostile to her child. This is often expressed in an over-concern which, like the over-stimulation referred to previously, has the effect of so loading the situation that the child, sensing her concern, is himself more anxious than before.

This may seem an over-elaborate and highly theoretical explanation

of the very common fact that small children are apt to make demands on their parents' attention. A corroboration which is often observed, however, is that someone outside the immediate family can often handle such a situation, once it has arisen, better than the mother herself. A nurse, in herself less aware of the difficulties than the mother, will still be able to approach the situation objectively, and manage the child without severity, largely because her relationship to the trio of mother-father-child is essentially from outside and not from within the family circle.

Equally common to observe are the jealousies and rivalries of one child for another. These may be based on the dispossession of the first child's unrivalled position by the arrival of a second baby, or on the greater powers of elder children, causing jealousy in the younger child. They are rarely due to actual preventable favouritism. Nevertheless, these situations require management, backed by understanding. In the minds of the moralists, jealousy and envy are usually coupled together. The link with pride is less often recognized. The child who is secure in achievement, and who is deriving normal satisfaction from the growth of his own powers, will very rarely suffer from any lasting jealousy. Where, however, the new situation appears to threaten his own security, and where that security to be so threatened lacks firm foundation, then jealousy may arise which will have a lasting effect on the formation of a child's character.

Nowadays it is unusual for mothers to go through with a second pregnancy without some preparations being made which include the first child. To do this may not be easy for the mother who is herself shy and ill-adjusted to carrying out her biological functions. Often in such cases, older children are quick to guess that something is in the air, and they ask ceaseless questions which are directed not so much to acquiring knowledge as to allaying their own fears of being replaced in their mother's affections. Such fear requires reassurance, and a safe rule to work on is that a child who knows enough to ask questions will have enough understanding to receive the answers.

Some awareness must precede the actual questioning and the answer may reasonably go as far, and no further, than the question. Children's birth fantasies tend to become terrifying to themselves when their normal curiosity is deflected and unsatisfied.

As a rule children are surprisingly ready to accept simple factual explanations. In giving them an explanation the mother is essentially including the child in the more intimate facts of her own life, which in itself goes far to counteract his impression that she is really going to discard him for another baby.

Equally important is to give him the sense of positive value in being his mother's oldest child, able to help her with a new and not nearly so able and clever baby. Such simple reinforcements as allowing him to lift and carry for her will go far to instal him in his new position.

Symptoms of jealousy tend to fall into two main groups: (*a*) Hostility and negativism; and (*b*) regression.

Hostility and negativism are commonly directed against the new baby, and particularly against the mother when she feeds him. Accidents due to older children, usually between two and three years old, actually attacking and damaging a baby are not unknown, and the situation must be faced, recognized and dealt with in a constructive way. It is not enough to scold the angry toddler who expresses, in the only way he knows, his fury at being replaced. This can only increase the deep feeling of guilt which he arouses in himself by this anger which is so much disliked by his mother that it threatens to cut him off still further from her love and care. He must also be made to feel that far from being unwanted he is a useful person in the nursery, able to do things for both mother and new baby. Jealousy is particularly apt to arise where a first child has been abruptly weaned because of a second pregnancy. Whilst such a situation may have been unintentional, a good deal of extra love is needed to tide over the crisis. Here again, the mother's difficulty will be much increased if she herself has feelings of guilt perhaps because a second pregnancy was not wanted at this stage. When this is the case, she can usually project and work off her own feelings in making the necessary preparations, concentrating on her delight in a first child becoming rapidly independent of her care.

Regression, by which is meant a going back to an earlier stage already passed and mastered, may, however, frustrate her efforts. It is quite usual for children who have already learned to feed themselves, or to go to sleep with the light out, who have control over micturition and of defæcation, to revert to baby ways of requiring help and care in these matters. Three factors must be recognized in this matter of reverting to an earlier stage. It is often supposed that the power operating is a conscious desire in the child to go on being a baby, *i.e.* behaving as one. This undoubtedly can be a motive, more often not at a conscious level, and always only part of the picture. When present, it serves to provoke the extra care demanded by the child's feeling of insecurity. In addition there is a positive and aggressive quality in some cases. Whatever method the child may select whereby he registers his discontent, the one certain to be effective is an urgent physical demand. A wet bed, dirty knickers, vomiting at a meal, or inability to sleep, will unfailingly produce attention if only because the situation created cannot be ignored. In considering what has been called the positive and aggressive aspect of such behaviour, it must be remembered that the small child possesses a very limited repertory, and can only claim his parents' undivided attention in a few rather crude but potent ways.

But in all these forms of behaviour, there is a very large element of anxiety, for which there may be a partly physiological basis in what is rather loosely termed " sympathetic imbalance." Certain individuals, far more readily than others, express emotions in terms of their bodily accompaniments. This is more likely to happen when sphincter control is a newly learned acquisition. Most adults are aware of moments of nausea in anxiety, and such expressions as " a sickening sight " have their physiological roots. Uncontrolled defæcation before battle is

a common experience in the front line. How much more likely the break-down during the vivid tension experienced by a small child whose performance in these respects retains a somewhat uncertain quality at the best.

Complaints are sometimes made that psychologists are over-tender in their handling of the defaulting child. Seen in the light of this explanation, it seems only reasonable to stress the unimportance of such physical mishaps, to reassure the child, and confirm his previous security, and to refrain from adding to his anxiety by making immediate success too important.

Much will depend on the initial habit training which has preceded the breakdown, and once more the wide range of individual variation in acquiring sphincter control is stressed.

Habit training.—Opinion differs as to when and how a child should be trained in normal habits. It is not a natural desire of children to be clean before they have any conception of the nature of dirt, nor have experienced the trained adult reaction to it. Most children are a curious mixture of the adventurous and the conservative. Many have a passionate preference for the same story, the same ritual, the same routes for walks, and their old familiar toys. At the same time they are driven onwards by their curiosity and their spirit of adventure into seeking new and unfamiliar ground. The double pull of safety and of adventure has to be appreciated in any study of the nervous child. There is, as a result of it, a strongly ambivalent quality attached to the discarding of one stage for the next. It is important also not to lose sight of the value to the child of an awareness of his own bodily excretions. To him they are part of himself. He enjoys the feelings they give rise to in his limited sensual experience, and he may often proffer them as gifts to those whom he loves. It is for him very perplexing that something so desired as a motion should be viewed with disgust when it is found in the bed and not in the pot, and his reactions may be confused and disturbed if his parent or nurse over-reacts to such an event.

Good habit training should result in a regularity which is so easy and natural as to pass unnoticed. It must aim at an acceptance of biological facts, and those caring for small children must be prepared to share and appreciate the child's natural physical pleasure in the exercise of all his normal functions. Control, imposed as a voluntary act of power, resulting in convenience and comfort for all concerned, will then become part of the child's creative activity. If habit training is too severe and restrictive, the child will tend on the one hand to be anxious over failure, and on the other to be aggressive in his refusal to exert control, or his refusal to relax and produce what is required. For the normal child some measure of control over excretions is gained by the end of the first year and many children are clean and dry by day at eighteen months. Urinary control at night comes later and is often not certain until four or five years old. Whilst no attention is paid to an occasional wet bed, repeated failure to be dry at night after the age of five should be regarded as a symptom.

Fæcal control is commonly gained around two years, and the breakdown is more often seen as an anxiety reaction or an obsessional ritual at a much later age.

Considerable variation occurs in the ability of children to learn to feed themselves, but with some help most two-year-olds can manage soft meals adequately with a spoon. It is interesting to watch the social effects of nursery school training fostering independence in a small child hitherto entirely dependent on his mother's ministrations.

Training a child to sleep is almost a contradiction in terms since the normal child sleeps when he is tired without any specific training. Common disturbances in the sleep behaviour are associated with teething and inter-current illnesses in the early years, with night terrors, especially in timid, excitable and under-nourished children around the two- to four-age period, and with nightmares, terrifying fantasies and refusal to be left alone in the dark, at the later imaginative periods, often reaching a pitch at the time of secondary dentition. The coincidence of these latter dates would appear to be fortuitous, and it is more likely that the nightmares occur with the emergence of the child from his sheltered home life into the welter of " big school " and the impact of other children.

Training, in all its aspects, consists in gradually educating the child into the social modes of his environment. Only when these are exceptional will difficulty be experienced in normal children. The actual time at which a child becomes dry at night matters much less than the associations he forms around the idea that he should be so.

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4. *ABNORMALITIES IN HABIT CONTROL*

Enuresis

The prevalence of nocturnal bed-wetting has been demonstrated beyond all question in the mass evacuation of children at the outbreak of war in 1939. It is of all children's somatic reactions the readiest and most easily provoked, as a protest and as a mark of anxiety and tension.

So much has been written as to the cause of enuresis that it seems likely that there is no single cause, but that it should be regarded as a reaction pattern which may be set in play by a variety of stimuli. Attempts to classify enuretics into groups of sympathetic imbalance,

status dysraphicus, hypothyroidism and the like, tend to prove disappointing since enuretics are manifestly not all of one kind. Hubert (1933) has perhaps the most definite contribution to make since he adds something to knowledge in pointing out the frequency with which there is a family incidence. Even this finding is questioned by Glennie (1950) working on a larger sample of cases, with controls. Many enuretics belong to the group of restless, hyperexcitable children so well described by Cameron (1945), but even this is not constant and among them are many who appear placid and stoical, only disturbed by their failure to grow out of this symptom.

Enuresis is in fact a symptom and not a disease. Many factors may contribute to its continuance in a child, not the least important being anxiety, tension and mental unrest. It is therefore worth while in all cases investigating from this angle, as the recovery from the actual symptom is not always in itself indicative of complete relief. Occasionally the reverse is seen where enuresis is cured, leaving the child irritable and extremely difficult to manage. Here it would seem likely that the aggressive aspect of incontinence has an important part in the clinical picture as a whole.

Treatment, because of the varied and complex ætiology, is apt to be disappointing. Most physicians find that their enuretics fall into three groups. There are a few who clear up almost at once on almost any of the many methods in vogue. There are a few who are resistant to all forms of treatment including deep psychological investigation. There is a very large intermediate group of cases who clear up slowly, in a way which seems to bear little relation to treatment at all.

There is no consolation to a busy and harassed mother, or an anxious child, in being told that the symptom will eventually clear up of itself. It is nevertheless true, and should be borne in mind whenever the merits of any particular treatment are assessed. Since there is no constant physical cause, it is a mistake to go in for elaborate investigations unless they form part of an organized research. X-ray for spina bifida yields interesting but contradictory results, and recent statistics suggest that the condition is at least as common in the non-enuretic child population as in the enuretics (Stalker, 1946).

Physical processes such as catheterization, or distension of the bladder with saline are to be avoided, since they emphasize the sense of physical inferiority and proffer a rather illusory hope of a physical cause and therefore a physical cure. It is, however, important to investigate the general physical condition very carefully, especially with regard to chronic catarrhal infections. Nutritional adjuncts such as glucose and malt and oil help considerably when nutrition is at fault. The urine should be checked for abnormal contents, and the very occasional incidence of diabetes, diabetes insipidus, and interstitial nephritis, should be borne in mind.

The general aim of treatment, having established a normal physique working under favourable conditions, should be to restore confidence. Children are often comforted by knowing that others do the same thing.

Mothers can be advised in such a way that they become less annoyed or less distressed at the recurring symptom. Some children are amused and stimulated by keeping a chart of their successful nights, but care has to be taken that this does not have the opposite effect of emphasizing the failures.

Psychological treatment should aim at uncovering deeper motives for this sign of unrest, and is particularly successful in children who have this symptom in association with a generalized anxiety, often with phobias and nightmares. In using play therapy, their interest in water play will often open up a fruitful and revealing fantasy.

Occasionally belladonna or potassium citrate appears to help and it is always worth trying ephedrine in doses of $\frac{1}{2}$ grain up to 2 grains or 3 grains in older children when it is well tolerated. Amphetamine in small doses seems to have a similar effect, but in prescribing either of these drugs the mother must be warned that as the dose is increased the child may become sleepless. This reaction to the drug varies with individual children and it should never of course be pushed further than to make the child sufficiently wakeful to be able to get up and attend to himself. Success in so doing makes him able to accept his symptom in a more hopeful spirit, thus forming the basis for a cure.

Other mechanical means, such as rousing the child during the night or limiting fluids, are again worth trying, but not to the extent of making the child uncomfortable or worrying the parent. Whatever is done must be undertaken with good humour and full co-operation from both sides. The only harm ever done by enuresis is done in an effort to cure the symptom, but in so doing destroying the child's confidence in himself.

Encopresis [1]

The problem of fæcal incontinence is, though less common than enuresis, still a good deal more common than was supposed, and a number of cases were brought to light in evacuation, when it became clear that this was one of the many ways in which children use their bodies as a means of expressing their feelings. It is uncommon for fæcal incontinence to persist quite unchanged from the napkin stage to a complete and daily lack of control over the anus. The usual history is that, after establishing cleanliness at a normal age, a breakdown occurs with a series of soiled clothes, after which the habit persists at irregular intervals. The initial breakdown may appear to be an almost deliberate regression, as when a four-year-old returns to soiling his clothes on the arrival of a new baby, or it may occur as a flag of distress, as was the case in many evacuated children, the soiling being quite unexpected and occurring involuntarily and without normal awareness on the part of the child. Some of these are intelligent children belonging to ambitious parents, who, while denying themselves, drive the child too hard, and immediate relief is obtained when this situation is seen and understood by both (Wyllie, 1939).

[1] See also p. 540 for modern views on bowel function and Hirschsprung's disease (p. 522).

Another quite different group of cases are older children whose incontinence appears to be part of a ritual. Clothes are soiled often with hard scybalous fæces and disposed of in odd places.

One intelligent girl of nine used to put her soiled knickers up the chimney; another very intelligent boy of the same age used to wrap fæces in paper and place them among his mother's clothes.

In these examples the symptom has no explanation other than a symbolic one, and the behaviour is in every sense dictated by fantasies at an unconscious level. Psychological treatment is apt to be long and difficult, but it is always highly rewarded, as the children in this group are nearly always clever and are exhibiting a number of obsessional mechanisms which, if allowed to persist, may form the basis of phobias or an obsessional neurosis, persisting throughout their lives.

In yet a third group, usually older boys, the habit is linked with anal masturbation. This may, but does not inevitably, follow on attempts at homosexual assault, which is naturally often difficult to prove or disprove.

In one boy the masturbation was observed during sleep and was followed by a reflex evacuation of the lower bowel. Treatment in this case uncovered a number of obsessional mechanisms and sadistic fantasies connected with his early, over-severe, habit training.

Fæcal incontinence should always be regarded as a symptom requiring psychological investigation and treatment. This may be as simple as a mere adjustment of the environment, and it may range to a long and complicated psychological analysis as in the obsessional cases, and it is noteworthy that occasionally the apparently simple case of incontinence in anxiety is uncovered by treatment, revealing underlying mechanisms of an obsessional kind.

Masturbation and other Compulsive Habits

No reference to childhood habit disorders could overlook the importance in the minds both of children and parents of masturbation which Cameron rightly and unequivocally relegates to the group of stereotypies, or compulsive habits. In calling them this, it is important not to lose sight of the psychic value for the child of all such habits, both in the symbolism attached to the symptom, and in the emotional conflict engendered in him by repeatedly doing something in itself pleasurable and associated at the same time with stringent parental taboos. Less dramatic but falling into the same group are nail-biting, head-rolling and banging, various sucking, chewing and biting habits, compulsive movements and some cases of stammering.

The essential quality, common to all these activities, is the repetition of an act to which there is a strong compulsive urge, with a feeling of tension until the act is performed, followed by a temporary sense of relief in doing it. The whole process of building up tension and discharge is repeated again and again, since the sense of relief is in its essence

temporary. When the act has been strongly forbidden, as it so frequently is, the whole process is accompanied by an emotional struggle, the effect of which is to increase the tension and need for outlet. When the habit is one of the minor peccadilloes such as nose-picking, it is usually done secretly, and nail-biting is often dismissed as being relatively inoffensive and therefore less highly charged with emotion.

It is often difficult to trace the onset of such habits, but they are exceedingly common in the small child, who is so limited in the means at his disposal for expressing and enacting his feelings. It must also be recalled that in infancy the child not only feels but expresses outgoing emotion with his body. Lacking language other than a universal cry, he kicks or screams or holds his breath or stiffens his body in a single mass reaction of protest. In much the same way, his pleasurable sensations are grouped around a few simple physical experiences, chief of which is sucking. Thus oral activities assume an importance later yielded, first to the excretory functions, and then to more directly genital activities. These in turn lose their significance as the intellectual outlets increase and multiply, although they revive again at puberty. Throughout the sensual life of adults the traces are visible of these primitive foci of emotional interest, and it is impossible to predict in which direction accentuation will occur. If it is accepted that all children go through these stages, then the later emphasis will depend a good deal on how satisfactorily each stage is experienced and worked through as it arises, making way for succeeding experiences of a different kind. When an impasse occurs, or when the infantile experience, say of biting the breast, is associated with considerable anger and frustration, the risk is run of perpetuating a need to go over and over that particular ground again in order to seek a consummation of the experience denied at the first attempt.

This tendency may then emerge as a chronic compulsive nail-biting, although all conscious association with breast experiences will be lost. Not every case of compulsive behaviour can be worked out in this way; often the clue to the particular choice of compulsion is missing, or there is too little emotional tension to motivate the search for an explanation. This is particularly true of some compulsive stammerers who accept their disability with a nonchalance comparable only with a true hysterical indifference or dissociation.

Enough has been said to indicate that while abnormal infant habits and experiences are not important in themselves, the way in which they are handled is important, lest they should become surcharged with parental emotion and thus become far too difficult and dangerous for the child to work off in the course of his normal development.

Dividing them broadly into oral, muscular, and genital experiences, it will be seen that the group as a whole is characteristic of the forms of experience most pleasurable to the infant. It may be held that genital experience plays no part in a normal infant's life. Nevertheless, many infants appear to discover for themselves pleasurable sensations from crossing and rubbing their legs and these not infrequently become

elaborated into what almost amounts to a technique of masturbation. The muscular movements, jerking, stretching and rolling are all characteristic of a healthy child and there can be no doubt as to the importance he attaches to oral sensations, using his mouth both for feeding and as a means of exploring many new tactile experiences. In children whose feeding experience has been satisfactory, the phase of putting everything into the mouth is usually quickly passed. Thumb-sucking can generally be got over by rolling the infant rather tightly in a shawl for sleep, and if necessary removing fingers or thumb from his mouth once he is asleep. This, together with ample experiences and adventures in other directions usually suffices to check the habit gradually without investing it with the joys of forbidden fruits. In the same way muscular movements are freely encouraged and the baby who is reasonably played with, and allowed to kick freely on a blanket, is less likely to develop muscular tics than one who is severely restricted.

Masturbation in the infant is naturally linked with adult sex experience in the mother's mind, and she has to deal with her own anxiety and repugnance before she can tolerate the habit sufficiently well to be able to deal with it in her child. Infantile masturbation usually passes quickly but may recur with the two- to four-year-old anxieties and again very frequently in the school years. Here it will inevitably link with some fantasy, and as a rule it is a cold, lonely and frightened child who masturbates itself to sleep, and not a sex maniac. A certain amount of judicious petting, with alternative outlets and free social activity, all go far to counterbalance the pull back into fantasy. If the child can talk about his imaginations so much the better, but any detailed treatment of the symptom is better dealt with in a child guidance clinic.

For the reasons which have been amplified in this section, it is important not to suppress a symptom without affording an alternative, and more socially constructive, activity. There is little use in increasing the child's sense of shame, since all these compulsive activities are fired off to some extent by anxiety. The symptom may be driven in, in the sense of being repressed to a still more primitive mental level, and will certainly be more likely to be concealed and indulged in privately. If the sense of shame can be excluded, the child can be more readily freed to play with things other than his own body.

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5. PSYCHOSOMATIC PROBLEMS

The psychosomatic is "a bodily disorder whose nature can be appreciated only when emotional disturbances—or psychological happenings—are investigated in addition to physical disturbances—somatic happenings." No illness in childhood is without its psychosomatic component. The infectious fevers can be taken as examples of those having the least psychic repercussion, whereas an integral part of many disorders, perhaps better regarded as reactive body-habits, is the psychic in combination with the somatic. Obvious examples are *asthma* and other allergies, the *periodic syndrome* in its variants migraine, cyclic vomiting, bilious attacks, or the hysterical recurrences and tics so common after the typical choreic attack, and the acquired psychic disturbance of the older enuretic.

Halliday outlines a six-point formula in support of the concept of the psychosomatic affection.

(1) Frequency of emotional causes as precipitating factors.
(2) Personality types associated with different affections.
(3) Sex ratios show marked disproportions in different disorders.
(4) An association with other psychosomatic affections.
(5) A family history of the same or associated disorders in parents, relations or siblings.
(6) The common phasic manifestation of the disorder.

Often it is impossible to say of these body-habits how much is due to inherited predisposition and how much to behaviour-training from parental precept, the "psychological infection." In all those showing an inherited predisposition an instability of autonomic nerve function is an obvious feature.

The common disorders of childhood with a strong psychosomatic component can be grouped to include inherited as well as acquired forms as follows on a modification of Halliday's classification. The largest group in childhood is the *gastro-intestinal*, displayed by rumination, mucous colitis and spastic colon, the habits of bulimia and pica, cyclic vomiting and other expressions of the periodic syndrome, lienteric diarrhœa, the mental state of cœliac disease, and anorexia nervosa. The *respiratory* forms are asthma and hay-fever; *genito-urinary*, enuresis which is probably the commonest of the functional disorders. The *nervous system* provides migraine, chorea, and some cases of epilepsy. Nor must the interrelation of organic, neurological and neurotic symptoms be omitted; the residual blemishes, latent or manifest, of organic disease, such as the over-excitability, fidgetiness, twitchings, tremor and minor motor disabilities seen in the less severe cases of birth trauma or following toxic and virus forms of encephalitis. *Mental* forms are revealed by the innumerable bodily disturbances developed during and as a consequence of anxiety states. These range in children from the common tics and habit spasms to the rarer hysterical paralyses.

In the *gastro-intestinal* group, *rumination* is one of the earliest neuroses to be acquired. The infant for whom breast feeding has failed and whose

feeds have been juggled between complementary and total feeding on a variety of proprietary foods perfects the technique of regurgitation and develops a perversion of taste or relish for the contents of the stomach. The perverse craving for more food or unnatural substances, coal, plaster, earth, known as *bulimia* and *pica* are due to psychic disturbance based on ill-definable abdominal discomfort of autonomic origin. Bulimia may, of course, indicate a lesion in the infundibular area, where so many autonomic centres are located. The *periodic syndrome* comprising bilious attacks, cyclic vomiting, bilious migraine and " recurrent pyrexia of obscure origin " (a revealing title) is certainly an inherited element. The children are usually of the hyperkinetic type, of good intelligence but who exhaust themselves, and in whose parentage a history of similar attacks in childhood, or of migraine in adult life, is a common finding. There is no hypoglycæmia in these children preceding an attack, the origin of which is nervous and the glycogen stores are depleted because of the symptoms, vomiting and pyrexia.

Lienteric diarrhœa is an exaggeration of the gastrocolic reflex occurring in the nervous child whereby as soon as food is taken (or excitement may act similarly) an evacuation of the bowel occurs. In cœliac disease the " moody, irritable, passionate and spoilt " temperament is partly due to the belly-discomfort of autonomic origin and partly in treated cases to the ill-advised attentions of the adult satellites daily consulting the invalid upon its dietetic whimsies. Whereas Simmonds' disease or atrophy of the anterior pituitary is rare in childhood, a " pituitary black-out " can occur with lowered metabolism, slow pulse, low blood pressure, pulse and respiratory rates, dry hair, harsh skin, and great aversion to food with severe emaciation. The psychic disturbance in such cases of anorexia nervosa is profound and probably precedes the organic signs.

In the *respiratory* group, *asthma* is found most often in children above the average in intelligence with a hypersensitive personality. They tend to be over-anxious, exacting, lacking in confidence, and stand up to tension poorly. The sex ratio is in childhood as three males to one female. The element of inheritance is strong. The power of the exciting element, or allergen, can be greatly augmented by an associated psychological factor, namely tension. Rogerson found the average intelligence quotient to be 108 in fifty chronic asthmatics, and 90 in a group of fifty controls.

In the group related to the *nervous system*, *chorea* predominates. Neustatter, in an analysis of the personality of the rheumatic child, was convinced that nervousness and hypersensitivity, preceded even the clinical manifestation of rheumatism. The sex ratio is decidedly greater in the female in chorea. Creak and Guttmann in a follow-up of hyperkinetic children found in the post-choreic a high incidence of nervousness, fidgetiness and motor disturbances, often in the nature of tics; in fact, a general motor instability.

To differentiate true chorea from the common habit spasm one crucial test is worth mention; the common tic is blinking, or momentary screwing up of the eyes, while the choreic facially expresses fleeting surprise by raising the eyebrows and never blinks.

Psychosomatic expressions of *mental* unrest in children are commonly the tics or habit-spasms. A tic is a psychogenic symptom, derived from brain disease, as in the oculogyric crises following epidemic encephalitis, or psychic factors—tension -in the constitutionally predisposed. In children they are seldom elaborate like the explosive utterances of coprolalic content in young adults -Gilles de la Tourette's disease—but more often psychic tics, repetition of words, echolalia, or of actions, echokinesis, or most commonly simple co-ordinated movements, eye-blinking, shoulder twitching, sniffing, spontaneous or originating from sources of peripheral irritation. Some cases of head-banging, head-nodding, body-rocking, thumb-sucking in infancy may be of this nature, but often when without any demonstrable association with rickets or ear-disease in normal as well as in mentally defective children they can only be attributed to a simple gratification in a rhythmic movement, and are usually without any sexual significance.

The hysterical palsies in children are always based on a combination of inherited instability and a state of tension. They are often acquired by imitation or follow a physical injury, and are usually of a simple character, flaccid or spastic paralysis of a limb, monoplegia, diplegia, or paraplegia. Exceptionally and only on a background of profound psychological disturbance do hysterical aphonia, ptosis, and amaurosis appear (Wolff and Lachman, 1938; Beverley, 1942).

Treatment.—In all the foregoing, psychological must accompany physical treatment, and is best given by the family practitioner in charge of the case. A knowledge of the family, of the inherited hypersensitivity, as well as an amelioration of the temporary causes of tension, will help to reform the bodily error of response in most cases. The pure case of asthma, uncomplicated by permanent pulmonary trauma, will respond as effectively to simple psychological treatment as to any other form of therapy, which, the more elaborate it be, is loaded with suggestive influences. For the hyperkinetic child who rapidly expends its reserves of energy, glucose in powder, $\frac{1}{4}$ to $\frac{1}{2}$ ounce, three times a day, as advocated by Cameron, is a useful prescription. The child who manifests any form of the periodic syndrome benefits from a prophylactic nocturnal dose of phenobarbitone, $\frac{1}{4}$ to $\frac{1}{2}$ a grain, and a daily simple rhubarb and soda mixture.

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6. *SPEECH DEFECTS IN CHILDHOOD*

Normal speech.—The vocal output of early infancy is produced involuntarily, and is limited to crowing, gurgling and to crying, depending upon conditions which are either pleasant or the reverse. Primitive sensations of bodily comfort, hunger or pain, are the chief factors in the

evocation of the suckling's vocality. The mechanisms for *voice* are already extant, the lungs or bellows, the vocal cords, and some simple reflex movements of palate, pharynx and tongue, but in step with the development of intellect the finer adjustments of lips, tongue and palate necessary for spoken language are acquired by imitation and by education.

In the first few months some modulations of the vocal tones, or the formation of vowel-sounds which are chiefly produced in the larynx, can be distinguished. By about the sixth month, a few consonants, labials—*p*, *b*, and *m*, and linguo-palatals, *d* and *g*, are being added to the vowel-sounds. In the second six months continuous experimental imitation rapidly enlarges the infant's vocabulary, and many words are used in definite association with concrete objects. The average child of two years is able to form little sentences in condensed or telegraphic style of noun and verb, can name familiar objects presented in concrete or pictorial form, and can obey simple commands. By the third year the use of pronouns and of a more fully stocked vocabulary extends the scope of the child's powers of expression. In the young child speech is almost solely centred on and stimulated by its own activities. Not until an age roughly between five and seven years does an ability for reasoned thought and argument begin.

Delayed speech.—In a few children in whom the ability to walk, to use their hands, and the signs of increasing intelligence proclaim to be normal, a lag in the development of speech even up to the third year is possible, but seldom later.

Feeble-mindedness of some degree is the commonest cause of delayed speech. To detect minor degrees of mental deficiency the surest way of assessing the intellectual state is by the standard tests in which verbal responses are not essential, by the Merrill-Palmer scale for the toddler and the Binet-Simon tests for children of school age. A complete interrogation includes the parents' account of the family history and of the child's personal history—the character of the birth and subsequent development in regard to sitting, standing and walking, and the occurrence of ill-health. Telling signs of mental inferiority are abnormal restlessness, inattention, and lack of discretion or an indiscriminate bestowal by the child of its affections.

Ill-health is a cause of delay in development in general, speech included. A sickly infant or one debilitated by a succession of illnesses is severely handicapped in acquiring speech, or may lose what ability it has attained, and not regain it until good health is re-established. Temporary states of aphasia are not uncommon in severe cases of chorea and as an aftermath of encephalitis complicating measles. *Tongue-tie*, so often put forward by a parent as the explanation for a child's backwardness in talking, might possibly be an impediment to sucking but never to the development of speech.

Deafness accounts for many cases of delayed speech. In the congenital cases the defect may not be suspected until the child is two or three years old, as the development in other ways is normal. Acquired deafness is the result of severe ear-trouble, or of cerebrospinal fever, or congenital syphilis.

A child with partial deafness is often said to be inattentive. The investigation of such a case includes examination of the ears for signs of inflammation, of the nose and throat for enlarged tonsils, adenoids and eustachian blockage; the mental state needs to be assessed and acuity of hearing is estimated roughly by the loudness of a conversational tone of voice needed to obtain a response and the attention of the child. More accurate information of the degree of reduction of the tone-scale, which is usually in its upper register in regard to spoken speech, is obtained by means of an audiometer test, in which in a graduated scale of loudness the names of common objects are reproduced. Wearing ear-phones the child reveals the level at which auditory reception occurs by pointing in a group of pictorial equivalents to the object whose name he has heard. From the age of four or five years a child of normal intelligence and partial deafness can start by lip-reading to interpret and reproduce speech satisfactorily. When a partially deaf child even sitting in the front of a school-class cannot follow speech correctly, he is better taught in a special school for the deaf.

Congenital word-deafness, a form of auditory imperception, in a child of normal hearing is a rare cause of delay in speaking. In most cases some degree of genuine deafness is actually present. The child is obviously intelligent and recognizes ordinary noises, but when spoken to appears inattentive and deaf. A sentence said over several times can be repeated parrot-wise by the child but without any sense of its meaning. The cerebral correlation between the centres of auditory reception and that for the interpretation of sounds appears to be undeveloped. Such children, with imperfect word-reception, respond quickly to training in lip-reading, by which means they learn to recognize visually words imperfectly heard.

Congenital word-blindness, a form of visual imperception, is a common condition. The child of school age appears incapable of learning to read. Even in a word of three letters, although the separate letters can be named, no sense is attached to their juxtaposition. The child is apt to be considered mentally deficient, but in other ways he can show his proficiency, especially in matters of manual dexterity requiring thought. Under individual tuition combining spoken with written language, plus pictorial illustration, the ability to read can usually be acquired.

Defective speech.—Some of the forms of defective speech, when persisting for longer than as a short phase in development, are more often found in mentally defective than in normal children.

Lisping, *lalling*, and *idioglossia* are minor to major defects in articulation of the consonants. Such defects in a child of normal intelligence commonly make their appearance in the second and third years, when the child begins to express himself in speech by an effort of will. In the earlier babbling stage when sounds are echoed by the infant without significance much less difficulty seems to be involved in their reproduction.

Lisping refers to the difficulty in pronouncing the consonants "th," "s," and "r," which are converted into "s" or "f," "th," and "w" respectively, and is common in normal children learning to speak. The more severe defect of substituting wrong consonants for ones over which a

difficulty arises is known as *lalling*, which defect if long continued is likely to be an expression of subnormal intelligence. Rarely a normal child appears to elaborate an unintelligible language of its own, *idioglossia*, due to the excessive replacement of consonants over which it has difficulty by others. In normal children these defects usually right themselves with the help of training at home and at school, but in the older child the help of an elocutionist is required to demonstrate methods of correct sound production and to prescribe simple exercises in pronunciation. It must be remembered that a failure to overcome lisping and minor degrees of lalling may be due to a habit on the part of the parents of encouraging the defect by imitating the infant's speech.

Echolalia implies the repetition of words in parrot fashion. Some degree of echolalia occurs normally in the infant from about the twelfth month when imitating the sounds of the last few words of a sentence, but without any understanding of their meaning. In older children of normal intellect the condition is rare and usually an expression of nervousness, but in the mental defective of low-grade echolalia is a common symptom.

Indistinct speech due to faulty articulation before the second dentition may be due to loss of most of the front teeth. A child of early school age who, by reason of dental caries has required extensive dental extractions, is severely handicapped in articulating properly. Other causes of indistinct speech are *nasal* speech, associated with marked enlargement of the adenoids and tonsils, and with post-diphtheritic paralysis. Proper articulation after operation for *cleft-palate* depends largely upon the resulting state of flexibility and reflex action of the soft palate. Some children post-operatively acquire normal articulation spontaneously, others require special tuition in learning to blow and breathe through the mouth. The chief defect is the replacement of the letter sounds "p," "b" (labials), and "d" and "t" (anterior linguo-palatals) by "m" and "n" with the voice escaping through the nose. Hysterical aphonia is extremely rare before the age of puberty.

Stammering.—The stammerer has difficulty in uttering certain letter-sounds, consonants more often than vowels, and "sticks silently" on meeting them, especially at the beginning of a word, while the stutterer repeatedly ejaculates the difficult letter—often one of the explosive consonants "p" or "b"—before completing the word. Stammering is far commoner than stuttering. Both are functional disorders of speech, depending upon a faulty co-ordination of three mechanisms, the lungs, the larynx and vocal cords, and the articulatory movements of the tongue, lips, palate, and jaws. The compelling cause is an emotional factor, disorganizing speech from its natural free flow without conscious effort into separate components to one of which exclusive attention is diverted. By the descriptive simile of John Wyllie (1894) in his book on *The Disorders of Speech*, the stammerer can be compared to the inexpert violinist, who, in concentrating upon the more difficult finger-stops—like the modulations in articulating—forgets the bow-hand, the producer of sound or vocal power as in expelling air from the lungs through the vocal cords. When arrested by a difficult stop position of the oral mechanism

for production of a letter-sound, the breath necessary for vocalization is either pent up by spasm of the glottis with subsequent explosive utterance, or is ineffectively expended. In the strenuous efforts in articulation, the stammering often shows an overflow of energy into other muscle groups. Thus, the face flushes and facial movements of grimacing, champing of the jaws, or protrusion of the tongue occur, or habit-spasms are developed, such as bizarre movements of the hands or stamping with the foot. A habit acquired by some stammerers to prevent arrest of speech is to utter a word on inspiration. A difficult initial consonant thereby is scarcely sounded, whereas the succeeding vowel can be sufficiently vocalized.

The neglect of the vocal element in stammering is readily explained by the fact that the consonants rather than the vowels give rise to trouble. The vowel-sounds are more intimately connected with the larynx, requiring voice from the passage of air from the lungs. In other actions demanding voice the stammerer becomes word-perfect, as in singing, declaiming, vocal imitations, and intoning. Stammering occurs when speaking in conversational tones, and is aggravated when conversing with strangers.

There is a much higher incidence of the disorder in boys than in girls. Among the predisposing causes emotional disturbance and instability are pre-eminent. A severe fright may provoke the habit. Heredity plays no part, but acquirement by imitation at home or at school is common. Left handedness is stressed as an important factor, and in some stammerers a history is obtained of an enforced shift from left- to right-handedness with consequent need of acquiring an alteration of cerebral sidedness. Similarly, in some cases, a retarded development of unilateral dominance with a prolongation of ambidexterity seems to exert an influence.

The onset of stammering can be observed at two age-periods. In young children of excitable temperament in their second to third years when speech is in an early stage of development stammering is common. No emotional distress is caused by the defect at this age. Simple measures of preventing and curbing over-excitement, and a gentle insistence on speaking more slowly are usually sufficient to effect a cure. It is in older children of school age about the time of the second dentition between six and eight years that the onset of stammering presents a serious problem. The growing emotional conflict is conspicuous in these cases, as shown by the overflow of energy produced by the habit, and by the disinclination to speak in public from fear of ridicule with consequent mutism and sense of inferiority.

In the *treatment* of stammering an explanation of the mechanism of speech production, suitable to the child's intelligence, must be given. He is first taught that sound can only come from proper use of the lungs and vocal cords, and that ample vocal power is present if he remembers to speak with plenty of *voice*. He should be encouraged to breathe often but not deeply or with exertion. Secondly, a simple analysis of the physiology of articulation is given. The letter-sounds of the alphabet are divided into groups in relation to the stop-positions of the mouth in producing them, and practice is directed to the articulation of such as give rise to difficulty. Vowels give rise to little difficulty as they

are produced with voice, and the stammerer is taught to emphasize them in speaking.

The stop-positions for most consonant-sounds in speaking are as follows:

(1) The labial—" p," " b," and " m."
(2) The anterior linguo-palatal—" t," " d," " n," " r," and " l."
(3) The posterior linguo-palatal—" k," " g," " ng," " y," " ch," " h " as in " here."
(4) The labio-dental—" v " and " f."
(5) The linguo-dental—" th," " s," and " z."

" W," over which difficulty often occurs, is to be practised as a double " oo," sounded as in " wool."

A short period of daily practice is prescribed on ascertaining which letters are difficult to articulate, short lists of words containing these letter-sounds are supplied. Confidence is increased by singing, declaiming like an orator, imitating, and by getting the stammerer to intone in reading aloud. By such methods he perceives that his speech can flow without impediment. The child who can read is encouraged to read aloud as part of his exercises, at first poetry for its euphony, and later prose. The co-operative pupil to whom such individual attention is given is likely to show marked improvement in his speech. It is doubtful if as much benefit can be expected from teaching stammerers collectively in special classes where imitation is likely to occur. In obstinate cases suitable training can only be given by a specialist in speech production.

7. *SCHOOL DIFFICULTIES*

What has been said in preceding sections will indicate how rarely difficulties in children arise *de novo*. They are grafted on to pre-existing situations, in which either tension between the child and his parents or his environment has arisen, or in which emotional experiences of early childhood have been imperfectly amalgamated into the structure of his personality and character.

It is easy to understand how certain epochs in the child's life will carry in them more potentiality for anxiety than others. This is particularly true of school, where for the first time the child comes away from parental support and sympathetic appreciation, and has to face on his own merits the range of uncompromising criticism from his fellows. All who have experimented with self government by children are surprised and shocked at the severity with which they treat the malefactor among themselves. Let no one for an instant suppose that children can afford strategically to be nice to each other. Of course they very often are, and the seeds of loyalty and altruism are there and flourish with all the expansiveness of free and happy childhood. But it is to be noted that it is nearly always in an atmosphere backed by adult control and approval that the child comes most readily to a happy exercise of his various capacities. Left entirely to themselves, children come too near their

own instinctual drives to be easy with themselves or tolerant of each other.

No one would on this account suggest that children should at all times be guided by adults, and it is therefore in his first group of children in the mass, as opposed to children who are his own friends, that the child meets with crowd hostility. If he is fully equipped intellectually, if his emotions are securely rooted in normal family life, and if he still carries intact his spirit of adventure and curiosity, he will meet it with his own particular methods and will continue to flourish and enjoy life. Look into the corporate activity of any school and it will be found to be seamed through with gangs and clubs and groups, with rules and sacred customs, all calculated to test the newcomer and protect the habitué. The awareness of this and the sensibility to appreciate it becomes the foundation of the adult's social sense. Into that adjustment may go many facets of the child's own individuality. He may react to discipline by becoming a slave to it, always requiring its support, or he may become a rebel. But by and large he will, during his school life, learn to live with people.

The child who enjoys the exertion of his intellectual faculties will tend to enjoy school quite apart from its social aspect, but when intellectual activity becomes a refuge from the pressure of social demand and an end in itself, then the child may be exceedingly unhappy in school, even though he excels in his lessons. Naturally, the child with personality difficulties will experience these in relation to all his activities, and in *The Nervous Child at School* Cameron gives a vivid picture of the effect of school life on maladaptation. Here, no attempt will be made to go beyond those difficulties which may seem to arise for the first time in connection with school.

Backwardness and learning difficulties.—Although progressive Education Authorities make every effort to provide suitable education for the subnormal child, it must be admitted that the dull child often fares badly in school. The remedy is essentially a social and educational rather than a medical problem. Dull children, however, are often brought to a medical practitioner for other reasons. Intractable behaviour problems, especially truanting and stealing, various manifestations of anxiety, sleeplessness and irritability, may all occur in the child who is really misplaced in his class. His inherent difficulties may have been overlooked by the teacher with a large class and his rebellion is sometimes fostered though not understood by parents who proudly say that they too never learnt anything in school, but got it all after leaving. It should therefore be an axiom that all cases with difficulties in school, whatever form these may take, should have an intelligence test, and if possible an educational test, to clarify the nature of their particular difficulties. Such testing should succeed in making quite clear whether this is a generally dull and mentally retarded child, or one with a specific educational problem, such as a difficulty with reading, or whether the case is one of a child with no inherent disability, but who is making no progress in school work on account of other problems of a temperamental kind.

In the case of the genuinely dull child, treatment can only be directed

to adjusting his education as far as possible to his needs, and to providing him with other ways of satisfying his urge to achieve, since the intellectual route is denied to him.

EDUCATIONAL DISABILITIES.—These include a group of children who have a persistent and unaccountable difficulty in learning to read. All the infantile ways of perception, which take no account of right and left, persist, so that confusions exist between letters capable of reversal, such as "b" and "d," and words like "was" are read as "saw." Writing includes a number of reversals, and at times the degree of distortion is so severe that the child writes a kind of jargon, often with certain perseverative conjunctions of letters. When intelligent, and they often are, these children show a marked preference for arithmetic and may sometimes excel in it.

The trouble lies in the fact that such children come to be regarded as stupid. They face the burden of chronic discouragement in relation to school work, and they are often driven to compensatory activities in truanting and stealing. Nor is the remedy easy to find, for the hours of individual coaching required to overcome such a difficulty are not easily supplied from the curriculum of any school with large classes. Sometimes these children are left-handed, or ambidexterous, and a history of lateness in establishing a preferential hand may give a clue to the clinical picture. These cases rarely reach the severity described by Hinshelwood (1917) as congenital word blindness, but in minor degrees they are not at all uncommon and account for a good deal of unhappiness in school.

Treatment may be almost entirely psychological since there will be an overlay of anxiety and a sense of inferiority, and many cases seem to relate to an infantile persistence which in itself is a symptom. Psychological treatment can sometimes be most effectively combined with remedial coaching. In this way, the child is aware of both direct and indirect help with his problem. Coaching without treatment, where a neurosis is fundamental to the problem, is apt to prove tedious and disappointing.

Similar difficulties seem to be experienced by some children in learning arithmetic, and conditions resembling Henschen's "acalculia" are observed. Since the need for mathematics is less universal then the need for reading, it is unusual for these arithmetic difficulties to go on to the accompaniments of discouragement and behaviour disorders.

INHIBITION OF LEARNING.—When there is a generalized inability to learn, coupled with a good intelligence on tests, it is always necessary to seek a psychological explanation. Very often it is a shy and socially maladjusted child who reacts in this way, or one with severe emotional difficulties generated from the home situation. Treatment should always be psychological, and whenever possible, removing the child from school for any length of time should be avoided, since it is often difficult to persuade him to return once he has succeeded in getting away. Some children in this group have nervous vomiting only in the mornings, and not on Saturday and Sunday, or truant with a white-faced persistence which witnesses to their extreme misery while in school.

PHYSICAL HANDICAPS.—Easier to understand, but surprisingly often

overlooked are the problems of the child who is physically handicapped. Whereas the severely deaf or hard-of-hearing child is catered for in a special class, as is the child with poor sight, little can be done for minor degrees of deafness and for the child in poor health or one who, through illness, has missed essential stages in schooling. Such children are competing in an unequal race, and the frequently chosen remedy of three months in a convalescent home will add to their scholastic difficulties, even while fitting them to deal with them. Physical handicaps which prevent a child playing games have an obvious repercussion on social adjustment, and this should be borne in mind when lightly prescribing what may seem to the active child the equivalent of a death sentence.

Stammering, though more a hysterical than a physical symptom, may suitably be mentioned here, since it constitutes a more severe problem during school life than at any other stage. During school years, the child who stammers is handicapped on all sides. He is teased or pitied by his fellows, and is the exasperation of the teacher who tries to get spoken work from him. His entire curriculum may come to be built around and adapted to his disability. (See speech difficulties, p. 1128.)

The aggressive child in school.—A rather easier problem than that of inhibition of activity is set by the aggressive and hyperactive child who has difficulty in canalizing his activities, and fails to apply his energies to learning. Such children are often said to be unable to concentrate, which is true, but leaves out of the description any idea as to why their energies are so dissipated.

Many belong to the groups described above as mentally inadequate, educationally retarded or poorly adapted to the social situation set by school. All these possibilities must be considered and any remediable defect removed before treatment is undertaken. The majority of these restless children are lacking in outlet, and being of somewhat dull intelligence, though having a misleadingly alert manner, they are more truly described as lacking in any capacity to utilize the outlets available to them. Often an improvement sets in when practical work, such as carpentry, is taken up, and a good club will take them off the streets in the evening. As a group they are often delinquent in order to pass the time rather than to serve any complex emotional need, and if they are fundamentally stable, with a reasonable home background, delinquents of this kind are often easy to treat almost entirely from an environmental approach.

Very different is the problem set by the unstable child coming from an unhappy or actually broken home. There the normal relationships within the family are so severely disturbed that the delinquency serves a dynamic purpose, though frequently not at the conscious level. A rather frequent association is seen in children with foster parents or step-parents, who steal as if they were symbolically taking what seems to them to be owed to them. Stealing of this kind is often done, not in a gang, but by a solitary boy or girl, taking goods which are subsequently given away as " presents."

The behaviour is not rational and the culprit appears genuinely puzzled by his own actions. While help directed to the environment may produce a temporary improvement, analytical treatment is usually required to

uncover the underlying mechanism. Problems of this kind will usually have their repercussions on school progress and it is rare for children with these more severe behaviour problems of an aggressive kind to do well in school.

An exception to this generalization may be made in the case of certain solitary delinquents, often with high intelligence, who after leading a model life, doing well intellectually, but living apart from the social group, suddenly break out into a series of almost fantastic crimes of an aggressive nature. One seems here to be dealing with a variety of adolescent fantasy, held strictly within bounds, denied any expression, and suddenly defying all attempts at further suppression. Such instances should whenever possible be investigated by a psychiatrist, for in some the outbreak may mark the onset of an adolescent schizophrenic illness.

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8. *PSYCHOSES IN CHILDHOOD*

Psychoses in children occur, and probably more frequently than was supposed. If the psychotic reaction is regarded as a mass attack on the individual as a whole, then it can be seen that in the affective psychoses a manic phase will involve a completely uncontrollable excitement, a depressive phase, a withdrawal into an aloof and non-responsive apathy, and the schizophrenic process of irregular splits in the personality will produce as bizarre a picture as in the adult, with the added danger that, being only lightly and recently integrated, the child personality shows little power of recovery from whatever constitutes the schizophrenic attack. The more severe forms of neurosis, such as anxiety states, compulsive states and hysteria, do occur in children, but they can always be related to the child's personality and to the environmental situation of the moment. In other words they can be seen as an attempt at adjustment.

In the psychoses, there is often little in the environment to warrant the severe reaction, and the observer is forced to suppose that the attack is comparable to an organic illness, arising from an unknown cause, or that it constitutes a response to difficulties engendered in the child's internal environment. By that is meant the world of his personal thoughts and feelings, his psyche, and the impressions so closely linked with that, which comes from his own body engendered by his physical needs and sensations. A study of the fantasies produced in play, in drawings and in the behaviour of a psychotic child, suggests strongly that this internal environment is of paramount importance in his psychotic experience. It

is an interesting speculation, therefore, as to whether this is so because the illness itself prevents the normal turning out towards external interests of a social kind, or whether there is something in the schizophrenic process which actually increases the child's awareness of his internal environment. Whatever the ultimate explanation proves to be, it is a matter of clinical observation that external events and stimuli pass unnoticed, and appear to have no interest or significance for the schizophrenic child.

One reason why so little is known of the psychotic process in the child is that the access to his mental processes is limited by the very state in which he finds himself. Another is that as the psychotic process in childhood is often irreversible, the end result can be mistaken for a severe degree of mental defect. Everyone who has had charge of defective children recognizes amongst the "aments" a certain proportion who are intelligent but psychotic.

Affective psychoses.—Manic-depressive psychosis is rare in early childhood. Kasanin found only four cases which developed before the age of sixteen years in a series of 6,000 patients admitted to Boston Psychopathic Hospital in the years 1923, 1924 and 1925, but it is possible that what was referred to earlier as a "withdrawal state" may in fact be a form of depressive reaction. Small children do from time to time pass through a phase in which they are silent and unresponsive, the condition being one of apparent apathy which must be distinguished from the frantic tears and protestations of the anxious guilt-ridden child. True manic excitement, with its characteristic flight of ideas, is exceedingly rare in the young child, and is again not to be confused with the wild excitability of the restless and unstable hyperkinetic child. Both manic and depressive conditions are seen in the adolescent and follow a course comparable with the illness as seen in adults.

Schizophrenia does undoubtedly occur in childhood, and it merges almost imperceptibly with the deteriorating psychoses of childhood such as those described by Weygandt as pfropf-hebephrenie, and by Heller as dementia infantilis. It cannot be too strongly stressed that much of the appearance of deterioration is due to the difficulty of access to whatever mental activity is going on.

The schizophrenic child develops normally up to a point. The onset of his illness is then varied, but it is likely that among the outstanding symptoms will be an emotional lability with unexplained tears or tempers, a progressive lack of interest in his surroundings, some regression in habits, either excretory or in feeding himself, an apparent deliberate turning away from normal social contacts, unexplained shyness and often rather odd and bizarre pre-occupations or unexplained fears. There is often a marked tendency to stereotypies whether of speech, manners or interests. A schizophrenic child may repeat the same grimace, or phrase, endlessly, or may reproduce the same figure in drawings. This may be related to poverty of ideation, or to a tendency to perseverate, characteristic of the mental limitation and rigidity so characteristic of psychotic states. The condition is often accompanied by a refusal to speak, and negativistic behaviour generally is quite usual. In patients who do not recover, speech

appears to be actually lost, and capabilities usually go in the order in which they are acquired. The output of "work," in the young child, the equivalent being his play, is progressively restricted, and he ceases to learn anything new. Sometimes the pathological process appears to be arrested at this stage, and after a period of disintegrated behaviour the child becomes able gradually to resume a more normal life. It is usual for many of the psychotic features to persist; these children tend to remain manneristic, their speech is often odd and stilted, and while some chatter to themselves, others retain their mutism or slowly re-learn a more normal vocabulary. Echolalia is common in this stage, and the child's facile repetitions may lead to exaggerated hopes. What is noticeable is that the child does not converse. He may respond, but he does not initiate any personal communication. Very often the disturbed sleep, the single-track interests and activities, and the inability to mix, persist, and it is at this stage that so often a diagnosis of mental defect is made. This is partly because the patient usually comes to notice for not attending school and if placed with mentally defective children will to the casual observer pass as one of them. But the more closely this group of childhood disorders is studied, the less is clear in regard to organic features, and no certain pathology has yet been described.

Yet another group should be included here, namely, the cases described by Kanner as early infantile autism. The disorder is apparent from a very early age and sometimes the child seems to have been different since birth, in that he has never developed any capacity to effect any human relationships. There is no abrupt change or falling off in capacity, but attention is often first directed to these children when, in spite of normal physical development, they fail to develop speech at the anticipated time. When it comes, speech is often fragmentary and contains features peculiar to the individual child concerned. Kanner regards these children as suffering from a disease *sui generis*, but makes no suggestion as to the pathological basis. Bender regards them as a variety of the schizophrenic process, characteristic only because of the very early onset.

Weygandt's pfropf-hebephrenie is really a schizophrenic illness grafted on to a border-line mental defect. Possibly the condition is really one of defect with psychotic features. Various authors, including Sante de Sanctis, described a "dementia præcoxissima" which again is probably an infantile schizophrenia occurring in so young a child that the disintegration occurs at a stage in which further learning is prevented by the disease process, thus giving rise to the impression of dementia.

Dementia infantilis (Heller) differs from these states in having a fairly constant clinical picture. Heller's monograph in 1908 describes six cases; by 1930 he had collected twenty-eight cases (Zappert, 1938). The onset is usually at the age of three to four, when a previously lively and intelligent child ceases to speak. At the same time, without any trace of inco-ordination, his movements become restless and purposeless. He is unable to play socially, becomes mischievous in an aimless manner, may lose control of his excretions and finally becomes an idiot. There are no organic signs, and deafness, which is the usual cause of loss of speech

in a young child, can be excluded. The condition is irreversible and these children usually end as untrainable, but apparently contented, inmates of institutions for the defective. Their restlessness and aimless destructiveness are constant characteristics.

Treatment offers no very dramatic prospect. Psychotherapy appears often to help the child to adjust but makes little headway, probably on account of the inaccessibility of the psyche to ameliorative processes. Convulsion therapy is something of a responsibility and therefore tends to be left only for patients in whom everything else has been tried. The results to date are disappointing. Removal from home is only justified when there are circumstances in the home which appear to have precipitated the condition, or where the child's state renders it necessary. Probably the best care that these children can receive is the undivided attention of an individual trained in child care, who will constitute a safe and comforting presence, and who will at the same time persist in her efforts to maintain contact with the disordered mind. In this way aptitudes and abilities can be kept awake, so to speak, and if there is a remission, full use can be made at once of any faculties which become again available to the child's purposive use.

Organic illness with an onset which produces a psychotic picture, such as juvenile G.P.I. and Schilder's disease, are described elsewhere.

Post-encephalitic behaviour disorder.—After the epidemics of encephalitis between 1917 and 1925, a group of cases emerged which were intensively studied especially in the U.S.A. The encephalitic illness was undoubted. The children had all passed through a febrile condition with one or other of the characteristic features of somnolence, diplopia, ptosis, nocturnal restlessness or choreiform movements. On recovery a profound change in character was observed. The restlessness persisted, with often wild excitement at night and periods of somnolence during the day. The character changes were most noticeable, among them a persistent tendency for these children to call attention to themselves. They were often spiteful and tale-bearing. Lying and thieving were common, and even in the face of indisputable evidence they would persist in blaming others for their own misdeeds. They were characteristically wildly impulsive, often dangerous in their attacks on others, petulant and querulous. In the slighter cases, where confinement was not necessary, they often showed a quite aimless impulse to wander off, and it was unusual for them to return from these truanting episodes without being in trouble of one kind or another. Sexual misbehaviour was fairly common, and their whole relation to society was characterized by an extreme irresponsibility.

Such cases were often said to have no organic symptoms, but a careful search would sometimes reveal a slightly immobile face, a cranial nerve weakness affecting perhaps one eye, or a slight Parkinsonism of one or both sides of the body. Tremulous lids or an inability to keep the protruded tongue out were also common. The most disagreeable feature of these cases was their imperviousness to treatment of any kind. Psychotherapy would appear to be effective and yet no lasting results were ever

observed. Hyoscine, belladonna or benzedrine, while for a time controlling the restlessness or the Parkinsonism when present, never affected the behaviour impulses, and it was found that segregation in a suitable school was the only means of control.

Not all attacks of encephalitis produce this gloomy syndrome, and encephalitic accompaniments, for instance of the exanthemata or after vaccination, may be without any result on the personality. Occasionally, however, there is a vague history of a febrile illness preceding some of the psychotic states described above, and it seems reasonable to suppose that an encephalitic component may be part of the less common infective processes in childhood.

Therefore, a history of fever, especially when accompanied by severe headache or drowsiness, or delirium and restlessness, or convulsions, should always be carefully looked for and noted in any investigation made on a child with a history of normal development up to a point with subsequent mental arrest or regression.

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9. *NEUROSES IN CHILDHOOD*

Enough has been said to indicate that many of the outstanding features of neurosis occur readily in the temperamental disorders of childhood. The impulse to repeat, and the guilty attempts to placate seen in the obsessional states, the dissociation of the hysteric, and the anxiety reactions, are all very commonly observed. This is understandable if it is accepted that the whole of childhood is a period of progressive adaptation from the purely self-seeking narcissism of the infant to the socialized creative activity of the adult, and if it is further accepted that all neurosis constitutes an attempt on the part of the individual to adjust to the pressure of circumstances.

In a certain sense it is perhaps true to say that what is a characteristic and necessary precaution or alarm signal applied in childhood, only becomes a neurotic symptom when it persists in the adult. The child *is* in danger from his aggressive fantasies when he is alone in the dark, and it is the child in the man, harking back to this situation, who is unbearably anxious in similar circumstances. For this reason, the terms obsessional neurosis, anxiety state and hysteria have been avoided, although there

have been frequent references to anxiety, to obsessional behaviour and to dissociation. Children do, however, sometimes show the fully developed features of a neurotic illness.

Anxiety states.—What has been said of the sources of anxiety in childhood will indicate that periods of anxiety are inevitable. It is only when anxiety is maintained over a considerable time, and is shown in relation to almost all activity, that the term " anxiety state " is justified.

Such states are usually the result of prolonged mismanagement resulting in the child becoming unable to approach any problem with confidence. Often the background will be a home in which parents are themselves neurotic and particularly when that includes an overt or concealed hostility to one another. In such a situation it is inevitable that their conflicts will prevent them from giving to the child any security from which he can in turn build up an adjustment. His values become confused because they are so often made the occasion of a tormenting scene between his parents.

Since a child must eventually work out his conflicts in relation to his father and mother, the removal of a child from home, even a bad home, to a home where he lacks both parents, is never to be lightly embarked on. In cases such as these, however, at least a period in a stable environment is necessary for adjustment to occur. Often a year or more in a home or school undertaking the care and training of maladjusted children is necessary in cases in which an anxiety neurosis has become a habitual reaction to the environment. Such care should, wherever possible, go hand in hand with psychological treatment.

Obsessional states.—Short periods of obsessional behaviour are commonly seen in most children. They probably serve a double purpose, by limiting experience to familiar ground, and by repeating an action which is symbolically significant until the emotional conflict which makes it necessary has been satisfactorily worked out.

Nevertheless, obsessional behaviour, unless very short lived and localized, should always be taken as an index of anxiety and an attempt made to discover its source. Compulsions as seen in childhood follow the familiar lines. A certain ritual must be followed in saying good night, every lamp-post must be touched, food must be arranged in a particular way, and such behaviour is often used to exploit the child's sense of power and his need to assert himself. In spite of the guilt attached to some rituals and the anxiety betrayed if the system be disturbed, the aggressive element in every obsessional's behaviour must be recognized if the pattern is to be understood. Often such rituals are elaborated in order to allay the fears arising from aggressive impulses directed against those whom the child both loves and fears. It is particularly important on this account to provide the obsessional child with plenty of outlet in which he can legitimately be aggressive. He may tear up waste material for his mother, burn leaves in the garden with his father, dig as hard as he likes, knock down his ninepins and so on, in this way linking his destructive impulses with his creative aims. This provides a more effective control than suppression or repression can ever hope to do.

Hysteria in children is here confined to a true hysterical dissociation and is not taken as including hysterical behaviour in the sense in which the layman uses it, in other words, as a description of a child in a tantrum or making a fuss.

Hysterical syndromes are not common, and when they occur they require careful differentiation from certain peculiar organic syndromes, such as for example those following an acute encephalitis. Conversion hysteria in childhood is a more dramatic state of affairs than in the adult, and if the diagnosis is made, it is absolutely incumbent on the psychiatrist to satisfy himself as to the mechanism. Being less articulate, the child will have fewer terms in which to explain his need for such a reaction, and treatment once attempted must be pursued until the symptom is completely cleared.

In a number of cases the hysterical pain or hysterical limp will follow an organic condition, often of a trivial kind. The persistence of the symptom long after the exciting cause has been removed is the situation which the psychotherapist must link with the mental mechanism at work, and as with the hysterical reactions in adults, it will represent " some gain which the illness brings in solving some problem, or fulfilling some wish, or in satisfying some desire in reality or in fantasy." (Curran and Guttmann, 1943.) It is characteristic of the hysterical reactions in general that the mechanism may be apparent to the psychiatrist long before it can be emotionally accepted by the patient, but until it has been recognized and accepted, no amount of explanation by the psychiatrist can help the patient to get rid of his symptom. In other words, he cannot afford to part with this prop to his psyche.

In the child in whom physical symptoms persist after the disease originating them has been cured, the motive may be one of gain in the way of sympathy and attention, or relief from tedious chores, but it is not usual for this mechanism to be operated consciously. Quite often the " gain " may be in a relief from anxiety. In spite of their nonchalance, children are usually disturbed by fears of death or disfigurement during an illness, and a persistent symptom may be associated with such fear, or may be an attempt to rehearse the worst that could happen as an unconscious reassurance. Children who are told not to shrug their shoulders or twist their neck as it will get fixed that way, do so again and again as if to gain the assurance that it still has not become fixed.

The forms taken by hysteria will vary nearly as much as in adults, but in young children hysterical blindness and deafness are rarely seen. A note of warning is sounded as to the great difficulty in testing hearing in a young and unco-operative child. Even an audiometer test may leave doubts as to whether a child is partially deaf or not.

Hysterical paralysis with or without anæsthesia is much more common than hysterical anæsthesia by itself. The loss of power may persist after a trivial injury or may cause some peculiarity of gait which may then persist as a habit. Hysterical fits occur, but less commonly than in the adult and are usually in the nature of a crisis, or an extreme rejection of some particular situation.

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10. *TREATMENT OF NEUROSIS*

Treatment will tend to fall into three stages. First there must be established a positive diagnosis of psychoneurosis, and in confirmation, any organic cause must be ruled out. In doing this, it is important to remember that the presence of disease may easily be suggested to a frightened child by unwise medical examination.

The second stage consists in the psychiatrist coming to understand the symptom in terms of its psychopathology and mechanisms. Thirdly, the physician must be able, by means of the rapport he is able to establish with the child, to convey the same degree of understanding to the patient. Put another way, he must enable the patient to feel free enough to share with the physician the realization that the symptom has a mental significance rather than a physical one. Both sides must do more than see it in this light, they must feel it, and the child must re-live the inadequate emotional experience which has led to symptom formation. He will play it out (literally), while he imposes first one rôle and then another on the psychiatrist. If, with this temporary support, the child succeeds in doing without a symptom, he has both admitted to himself, and shared with the therapist the knowledge that his symptom is in the nature of an adjustment which has failed.

Naturally enough, none of this is admitted in so many words, and with younger children the stage of verbalizing an explanation is often never reached. The mechanism of a psychoneurosis may be demonstrated in play, but in many cases even this implication is lacking, and the physician is left to infer from the child's improved behaviour that an adjustment has taken place. When this is so, it is important that the psychiatrist should not impose his own verbalized explanation too readily. Verbal acceptance means so little to a child, whereas the emotional realization of a situation in play is of fundamental importance in effecting a cure.

Where words are of use is in making clear to parents or teachers just how an attitude, or certain behaviour characteristics, can be related to a child's emotional life. Here again, it is wise to wait for the demonstration in fact, before proceeding with the theoretical explanation. If a child's difficult behaviour threatens the parents' self-esteem, as it so often does, the explanation will be eagerly sought by them, but when produced prematurely, will be refuted again and again. Here too, will be seen the need for reassurance; an explanation can only be accepted by an individual who is secure enough to face its implications. When that stage has been achieved there will often be no need to make the explanation.

Methods of treatment are bound to be determined to a large extent by external circumstances. Psychotherapy must take time, and is quite uncompromising in the demands that it makes. Unpunctuality, forgotten appointments and inability to meet the psychiatrist's demands are often part of an emotional resistance. On this account, it is of the utmost importance to take time over the initial diagnosis and summing up of the case, so that some idea of these demands can be given early on. Glib promises of an early adjustment, which are followed by disappointing progress and ever increasing time wanted for treatment are apt to lead, not unreasonably, to the supposition that the case has been mis-diagnosed, or that it is being ineffectually handled. An outline of *how* progress is likely to come about is more valuable than unsound prognostications as to *when* the child will be cured.

It is important to keep in mind the fact that a number of cases clear up quickly and decisively and, it must be admitted, often do so unexpectedly, for no apparent reason. There is therefore no need in every case of childish maladaptation to embark on an elaborate therapeutic programme before the simple and obvious remedies have been tried. These resolve themselves into adjustments of the environment, physical aids where these are indicated, and the emotional re-education, without which none of the other methods of treatment will have any effect.

It is extremely difficult in any outline of child psychiatry to indicate the kind of case in which superficial treatment is likely to be justified. It is justified whenever it is effective, bearing in mind that the mere suppression of a symptom may lead to its reappearance at a later stage or in another guise. Anyone who has had wide experience of enuresis will remember the cases in which the bed-wetting cleared up and was followed by temper tantrums, night terrors, and not uncommonly by stealing. Clearly the enuresis must have served in some way as an emotional vent, and the tension caused by removing the outlet results in a different manifestation of the same tension. This sort of outcome tends to follow an inadequate initial exploration, where synthesis is attempted before analysis is complete. It is rather as if an attempt were being made to do a jig-saw puzzle without first taking all the pieces out of the box. Hence the emphasis once more on the fundamental importance of the first exploration being as thorough as possible, however simple the case may seem at first sight.

In exploring the environment, recognition must be given to all the factors. An excellently run institution may, in fact, constitute a thoroughly bad " home " seen from the emotional angle ; and conversely, a home which is bad from the economic angle may be a perfectly good environment for the emotional growth of the children in it, even if their bodies suffer from its inadequacy. Physical facts are the easiest to establish, but they should never be accepted as more than part of the story. Herein lies the value in taking a history first hand, where so much more is told by the manner in which facts are given.

While the outline of the story is in terms of a description of the child, of his symptoms and the circumstances in which they are manifested, of

his health, his general development and of his relationships at home and at school, the essence of it will be revealed in small allusions and in trivial comments by the way. The mother who described how carefully she boiled tinned pineapple before giving it to the children, was revealing a great deal more of her domestic history than she realized. Is it in fact unsound to deduce that she was unduly concerned over the children's health, guilty with herself at yielding to their unhygienic preference for tinned food, credulous in her attitude to advice and at the same time insensitive to common customs, a woman inclined to bring up her children anxiously and " differently," apart entirely from her fundamental ignorance of the processes involved in canning fruit ?

Treatment then will begin with a history, which, to borrow a phrase from another context, will have its manifest content of facts and its latent content of feelings. It is no exaggeration to say that treatment begins with the taking of a history, for while that is being done, the relationship is built up which makes it possible for the mother to admit to her difficulties and accept the physician's advice. The same is equally true of the relationship between the physician and the child, who, after all, is the patient. Because so much depends on the work which the physician does with the parents it is often supposed that treating nervous difficulties in children resolves itself into treating the parents. This is quite erroneous and fails to take into account what was said at the beginning of this section, that the child himself is an individual and that his symptom is his own, albeit unsuccessful, attempt to deal with adverse circumstances. It is true that the circumstances may be adverse to him because of his particular and personal difficulties, or they may arise from emotional problems which are so entirely his own that he may be said to be creating his difficulties. In either case, treatment must be given in such a way that it includes both the parent and the child.

The problem facing the family doctor or school medical officer is the decision as to when a case which is in the main a nervous problem should be referred to a psychiatrist. There can be no hard and fast rule for this, and the fact remains that even for the expert an apparently simple problem may prove to be part of a deeply founded maladjustment, while occasionally the reverse is true, for the most florid symptoms and misbehaviour will sometimes yield at once to a very simple readjustment. Broadly speaking it can be said that so long as the situation is rightly apprehended, either can be tried depending on the availability of expert help.

A simple readjustment which is attempted and fails, does not prevent deeper treatment at a later date being successful. A more difficult case, referred to a Child Guidance Clinic, may be seen once or twice and returned with advice for future care, and it need not be supposed that psychiatric opinion will necessarily involve a long and complicated analysis.

But just because it may do so, the initial investigation must be thorough. It will include an estimation of the intelligence, and exploration of the home circumstances and the mother's attitude to the child, and the full understanding of the resulting problem in the child may only become

clear during and through the process of treatment. It is therefore fitting to conclude this section with an attempt to give a picture of what happens in treatment.

Because of the fundamental importance of approaching the problem from these three aspects, social, psychometric, and personal, it is usual for the child psychiatrist to work as a member of a team, which includes a psychologist and a social worker. This division of labour may seem over-elaborate, but it is difficult to see how otherwise the initial assessment of the case can be full enough to make even simple treatment effective, and it sets the psychiatrist free to undertake the actual business of treatment. If psychological help in childhood is able to prevent maladjustment in adult life, and it certainly should, it needs no further excuse.

The rôle of the psychologist.—Mental ability is composed of many facets, and to assess a child's mental age or intelligence quotient as a simple figure is a very crude approximation. What the psychologist must do is, by a series of tests, to determine how far the child's ability is up to the average for his age, whether it is evenly developed, whether it lags in some respects, or is precocious in others, or whether a general or a particular lack of ability and delay in development is responsible for his behaviour problem. It is of little use punishing a boy for repeated petty thefts, when the real situation is that he is a big husky borderline defective, quite unsuited to ordinary school and unable to cope with it. At a disadvantage there, he compensates for it by activities in other directions. While the police may consider him "sharp," it really requires very little basic intelligence to steal from one of the big stores, and such a situation only becomes intelligible when the school difficulty is taken into account. Whilst a large part of the psychologist's contribution lies in spotting these instances of poor ability, he is equally valuable in being able to demonstrate instances of ability which have been overlooked. Nothing is easier than to mistake a dreamy and self-absorbed child for a dullard in a large class, where such a high premium is placed on social adaptability. Recognition of latent ability of this kind at once determines the lines upon which treatment must proceed.

The rôle of the social worker.—The social worker, on the other hand, is available for a variety of contacts, with the mother in the clinic, with the home as such, with the school or the police or the probation officers, and her view will fill in all the details of what may be quite a complex background. The physician will then have a picture of the setting of the problem which he would be unlikely to obtain without this help. To the social worker falls the difficult job of communicating all this, as a dynamic factor, to the physician, and in turn she must interpret his findings in treatment of the child to the mother. No treatment can be effective unless the people who play a part in the environment can, as it were, keep pace with it in their understanding. This may almost amount to an education, or at least a re-education of the parent, in order that she may be ready to accept an altered attitude to the child and his problems now being resolved.

The rôle of the psychiatrist.—First and foremost, armed with his outline

of the situation, the psychiatrist must establish contact with the child. This will not necessarily be a contact with the orthodox child standing before him, well-defended and aware of what he should say and do. His essential contact must be with the other child concealed behind that façade, a being so unorthodox, so wild in his actions and so turbulent in his feelings, that he exists as a menace and a shadow, to be feared and ignored whenever possible. If the physician can be allowed to make his acquaintance, it will be the first step in the child's acknowledging the existence of such a demanding and untamed streak in his make-up. This recognition and acknowledgment is unlikely to take place at a verbal level. For this reason, the psychiatrist deals with the child's psychic material by means of play, in other words, in terms of his fantasy, which is a medium which he must understand and handle with familiarity. The child under treatment may use make-believe, or drawings, or modelling, or building, but in whatever he does, he includes the psychiatrist as a play-mate and shares with him the feelings which he reveals in his play. If the psychiatrist accepts a purely passive rôle of watching the child at play, he may succeed in understanding the nature of his difficulties, but he is unlikely to succeed in resolving them.

Readjustment often comes about when the child, having played a solitary and revealing game with the psychiatrist alone, becomes able to join as a socialized being in a group of children at play. His reaction to the group, and their reaction to him, will do much to complete what individual treatment has begun.

With older children, the process of treatment may of course be more highly verbalized, and with adolescents will be very little different from the psychological treatment of adults. Here there will be occasional cases when suggestion, with or without hypnosis, will be required, and when occasionally the technique of narco-analysis may be utilized. So long as all these are regarded as short cuts imposed by circumstances and not the method of election, the need for full understanding and co-operation on the part of the child will not be overlooked.

Medicinal treatment plays a small rôle in child psychiatry. In all cases it is naturally necessary to establish as good a state of physical health as possible, and minor physical defects should always receive attention. Occasionally, sedatives will be required to tide over the most acute stage of a sleeping difficulty. Some enuretics are greatly helped by ephedrine or benzedrine, and so long as it does not fool either the psychiatrist or the patient as to the level at which it helps, it should be used as fully as the response to it justifies. Nor should the great relief which is afforded to some children by glucose be neglected. It may succeed in tipping the balance in the favour of a weedy and anxious child, trying desperately hard to deal with conflicts of one kind and another. By prescribing it to help, and not to cure, the physician is doing all he can to assist nature.

Nevertheless, the essential problem of maladjustment in childhood remains an emotional one, and only those measures which are prepared to accept and reckon with this, will succeed in curing the child and relieving his parents' anxiety on his behalf. The physician will remain

the whipping post for both sides, and his own emotional understanding of the problems will be ultimately his only weapon in dealing with them.

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11. *MENTAL TESTING IN CHILDHOOD*

One of the items in the most widely used intelligence test of the present day refers to a proverb which runs : " Large oaks from little acorns grow." In 1905 an acorn, the germ of this intelligence test, was planted in France by Binet and Simon for the detection and demarcation of feeblemindedness. During fifty years or so it has grown into a tree which spreads its branches over the whole civilized world. Among the vast number of tests in use to-day the Binet test, as it is popularly called, is a nuclear test embodying basic principles of mental measurement in children. It has been through several revisions in English, the latest being that of Terman and Merrill in 1937. This has two equivalent forms, L and M, each containing 129 items. Form L is the one most used, and Form M is designed for re-testing children after a short interval.

This test has been translated into many languages. In its present form it ranges in difficulty from items which the average child of two can just about cope with, to those which only the " superior adult " can do. For the early years the test material consists of toys, pictures, bricks, beads, etc. ; though the ability to understand language is involved almost from the beginning. Later, the items take on more of the question and answer character, and call for the exercise of reading, general knowledge, reasoning, judgment, memory, vocabulary.

This type of test, one of many different types, is called an age-scale because it is divided into sections for each year of age. Success in a single item earns from one to six months of " mental age " according to its position in the scale, *i.e.* one month from year two to year five when mental growth is rapid and when a few months of mental age represent a big step for a small child, to six months after year fifteen when the superior adult has to be assessed. (In present practice the test is hardly ever used for adults.) The sum of the successes is the child's " mental age." A further calculation will give the child an " I.Q." or intelligence quotient, which is an index of brightness and also a guide to the rate of mental growth. The formula for the I.Q. is :

$$\frac{\text{Mental Age}}{\text{Actual Age}} \times 100$$

Thus, if a child of ten has a mental age of six, his I.Q. is 60, and he would be regarded as mentally defective. Had his mental age been fifteen his I.Q. would be 150, and he would be regarded as of superior intelligence.

Recently a new type of test for children, based upon a highly successful scale for adults, has been published, the " Wechsler Intelligence Scale for Children " (1951). The items are not in age-groups but in sections according to subject-matter. There are five " verbal " tests, and five " performance " tests, and separate I.Q.s are available for each main division as well as for the full scale. Scoring allows for grades of answer, which is an improvement on the success-or-failure marking. The scores reflect, broadly, the theoretical-practical bias in a child, and, in addition, the ten sectional scores are converted into a common notation which allows comparisons to be made between the sections. In graphic form this constitutes a " profile " of abilities which shows at a glance the general pattern. In method and scoring this test is quite different from the Terman-Merrill test, but it does not replace it. Each has its special value and each its adherents. It is an advantage to have both on hand in the clinic.

Mention has been made of " performance " tests. Early tests of intelligence favoured the academically-minded child, and various manipulative tests and scales were later introduced to offset this bias. To arrive at an all-round assessment of a child it was considered desirable to use both types of test. For example, children are known who were subnormal on the verbal type of test, but who came out well above the average on pictorial-manipulative tests, such as fitting missing pieces into pictures, tracing mazes on paper, copying a series of designs with coloured bricks, fitting wooden shapes into correct insets, and similar tasks.

Two interesting developments in the " psychomotor " sphere are the " Oseretsky Tests of Motor Proficiency " (1946) and the " Van der Lugt Psychomotor Test Series " (1949). Both depart from tradition.

The Oseretsky tests are grouped into an age-scale as is the Binet type of test, and there are tasks for both boys and girls throughout the age range from four to sixteen. At the lower end of the scale the child may be asked to clasp the examiner's hand or to raise his eyebrows without undue superfluous muscle movement, whilst at the upper end the child may be required to carry out a rather complicated task involving balance and co-ordination of the whole body. In essence it is a scale of agility and dexterity which a psychiatrist or psychologist might regard as outside the scope and requirement of a child guidance clinic, though it may have interesting research possibilities.

The Van der Lugt scale makes use of hands and fingers mostly and is done by the child while sitting. It is divided into a series of tasks and norms are available for each, on a sample of children between the ages of six and thirteen plus. There are exercises for both hands simultaneously, or for the preferred hand only, involving pressure, balance, co-ordination, speed, and accuracy. It does not call for the amount of brainwork which is involved in some of the earlier " performance " tests, but it does indicate whether or not a child is " good with his hands."

Intelligence may, for convenience, be divided into theoretical, practical, and social. Tests for the first two have been mentioned. The last-named is the most difficult to assess by objective methods, but some attempts

have been made, notably in the " Vineland Social Maturity Scale " (1935). This scale lists a large number of things which are characteristically performed by children of different ages, such as shopping alone, using the telephone, and many others. For much of the information the examiner is dependent upon someone who knows the child well, and who can give an unbiased report. The total assessment is in the form of a " social age," and, of course, the list can be scanned for more detailed information on the child's social aplomb. The scale is probably more influenced by the child's cultural *milieu* than any of the tests so far mentioned, and certain items would have to be left out for children living in most countries other than the United States.

At this juncture it should be mentioned that the I.Q. or any other numerical measure of a child's abilities is not to be regarded with the same confidence as, say, a measure of his height or weight. It tends to vary within limits, like a galvanometer reading. The test result is a complex affair, affected by many things. It is affected, for instance, by the child's upbringing and education, his temperament, and his condition at the time of testing. The attitudes and abilities of the examiner come in as well. Also, a test only samples a child's abilities, and he may well achieve a different result on another test.

Generally speaking, if all conditions are satisfactory, the I.Q. tends to remain fairly constant through life, *i.e.* the child tends to maintain his position relative to his fellows. A good test, therefore, reliably done, may yield a useful prediction of future prowess.

Emotional interference with test results can be detected by the examiner, not only by observing the child's behaviour in a standard situation, but also from the pattern of successes and failures and other signs in the test record.

A child's I.Q. will locate him in one of the following categories :—

	I.Q.
Very superior	131+
Superior	121–130
Above average	111–120
Average	91–110
Below average	81– 90
Borderline defective	71– 80
Mentally defective	70 or below

The intelligence test was the earliest type to be used in clinics, and is still the basic test. There are many others, however. A modern year book of mental tests lists some thousands of them (Buros, 1948). They fall into one or two main divisions, such as the scholastic tests in practically all subjects, covering the whole period of schooling : aptitude tests for use in vocational guidance (finding a suitable job for the person), and in personnel selection (finding suitable people for the job) ; personality tests, and a great many tests of more specific functions such as memory, attention, imagination, reasoning, persistence, suggestibility, honesty. Many of these tests emanate from research sources. Research in psychopathology includes the design and application of tests to different diagnostic groups to see if differential patterns emerge.

The newest, and perhaps the most interesting, of the above fields of work is that of " personality " assessment. All sorts of techniques have been proposed for this difficult task. There are the self-assessment tests such as the questionnaire which the subject fills in himself—obviously suitable only for older children—and other types where the information is obtained indirectly from the test material. Many tests, as mentioned, set out to measure fairly definite traits, whilst some claim to measure more general traits such as neuroticism, temperament, or character.

Much work is being done in the field of " projection " tests, in which the subject, by responding to material such as pictures and inkblots, and expressing himself through the medium of story-telling, drawing, or acting, unwittingly projects his needs, fears, and attitudes into the situation. Some of the better known of these tests are the following :

The " inkblot " test, used intermittently at the beginning of the century, but standardized and made into a remarkably useful technique by Hermann Rorschach, a Swiss psychiatrist, in 1911 (Rorschach, 1932), is perhaps the best known. The subject is shown, one by one, ten standardized cards bearing printed facsimiles of original inkblots, and is asked to say what they remind him of. The responses are recorded verbatim, and are marked in accordance with an intricate system which takes some time to master. From this and the actual content of the subject's remarks a personality sketch is derived. This is partly objective, and partly subjective. If the examiner has good insight, and a fair experience with the technique, he can derive valuable information about the child. Subsequent versions allow large numbers to be tested simultaneously, but the information gained is not as full as in the individual test.

Another widely used technique, as old as the last-named but much more recent (1935) as a standardized technique, is the thematic apperception test by Murray (1947). Specially selected and specially drawn pictures are presented to the subject. Most of them present human beings in various groupings or situations, and the subject is asked to weave a story around each picture. Children take readily to this test. Their pictures, of course, are different from those of adults. Again, it is assumed that the child, in his stories, will project his own wishes, anxieties, and opinions. The marking of this test is more subjective than that of the inkblot test, and the examiner must be always on the guard against the " personal equation " coming in. A quantitative method of marking has been involved, but it is tedious and of doubtful practical value.

The " world " test (Buhler and Kelley, 1941) offers great possibilities in the clinic. The material consists of a large number of toy objects representing people, animals, and inanimate objects with which the child can build a farm or a community. What the child does—or fails to do—with the materials is often very revealing about the child and his problems. Since he tends to act out and verbalize his phantasies in this kind of situation, the test is useful during treatment sessions.

Drawings and paintings have been used for many years as sources of information about children, and one very good test—the " draw-a-man "

test marked on a scale of points which follows the natural development of a child's drawing from infancy, was used as an intelligence test. Personality pointers have also been derived by Machover (1949) from a child's drawing of a man.

Other personality tests may be mentioned very briefly :

The word association test, one of the oldest of clinical methods, asks the child to reply with the first word that comes to his mind each time the examiner says a word. The reactions are usually timed, and any word which disturbs the subject's emotional equilibrium can usually be picked out without any difficulty by various signs associated with it, such as a long reaction-time, signs of discomfort, an obvious substitute reaction word, and so on.

An interesting variation of this method is the sentence completion test (Rohde, 1947). The subject completes such phrases as " I'll never forget . . .," " What puzzles me . . .," " If only I could. . . ." Records accumulated up to date show that some very revealing material can come out of this test.

A fascinating development of recent years is the mental assessment of the pre-school child. For this purpose there are many shorter tests, and a few complete scales which range from a few months of age to six years or so. It is, perhaps, invidious to select from this material, but the following have become firmly established in clinics.

The Merrill-Palmer scale (Stutsman, 1931), with a range from eighteen months to six years, is often used instead of the Binet test for these years. The two together form a useful selection from infancy to late adolescence. The former was specially designed for the pre-school child, and has a great many more items for this period, most of them being pictorial or manipulative. The scale is pleasant to administer and the " toys " are attractive to children.

The Buhler scale (Buhler and Hetzer, 1935) is basically similar to the Merrill-Palmer scale but, though published in English, it lacks adequate English norms, the test being originally standardized on Viennese children.

The Gesell scale (Gesell *et al.*, 1940), like the last two, is an age-scale, but it covers a wider range of activities. It is based upon observations of what normal children do in natural situations. The fields of activity covered through infancy are those of " sense-perception, posture, prehension, learning, language, and social." These are what might be called the latitudinal aspects. Longitudinally, certain " key " ages were selected as points of reference, *i.e.* the supine, sitting, locomotor, and pre-kindergarten, and norms for these ages are supplied. The scale is described as " an appraisal of the maturity of the nervous system with the aid of behaviour norms." The scored record gives a " D.Q.," or developmental quotient. Pædiatricians are familiar enough with the normal " milestones " of development in children, but with this scale they may assess maturity in much more detail and with much more precision. In their monumental work at Yale, Gesell and his collaborators have studied hundreds of children, both normal and abnormal, and have published lists of some of the common developmental anomalies caused by birth injuries,

amentia, neurological and sensory defects, toxic illnesses, and other conditions (Gesell and Amatruda, 1947).

In conclusion, something should now be said about the uses of mental tests in the child guidance clinics. Apart from schools these clinics are the most consistent users of tests, and in a more intensive way. Most school tests are given to groups of children, but in a clinic this rarely happens; it is neither feasible nor desirable. The individual testing, where the child and the psychologist work together, and where the latter is able to change his approach to meet the demands of the situation, can give much more information. In a well-staffed clinic, every child would be tested as a routine.

Many children are referred to the clinic because they are not getting on well at school. In these cases the psychologist will first of all want to know whether or not this is due to subnormal intelligence. He will also wish to check the alleged backwardness by suitable diagnostic tests which throw light on specific weaknesses, particularly in the "three R's."

Delinquent children, referred by the juvenile court or probation officer, will need to be tested to see if their misdemeanours are due to low intelligence or not, and one or more personality tests may be desirable in these cases.

Special clinical tests may be used in cases where cerebral damage is suspected. One research school in America specializes in this field (Strauss and Lehtinen, 1950), *i.e.* in the diagnosis and education of brain-injured children.

Testing children individually is an art. Some take to it readily; others never make a success of it. Perhaps the most difficult task is that of testing the pre-school child. He is not yet used to sitting still in a chair for anything up to an hour and performing tasks at somebody's behest. The tester may have to discard the standard procedure in favour of a method which puts material in the child's way as opportunity occurs, in the hope that enough will be done to allow a reliable report to be made. If the child cannot talk he will be given non-verbal material, and if he is deaf or unable to understand language the test has to be administered by gesture.

Nowadays, mental testing plays an important part in child guidance, and, therefore, in pædiatrics. Where the clinic is attached to a children's hospital it can contribute towards a psychosomatic approach to the problems and diseases of children.

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12. *THE EPILEPSIES*

Introduction.—The multiple forms of epileptic seizure are familiar to anyone in the practice of medicine, but the problem of what constitutes epilepsy has yet to be solved. " The epileptic fit," Kinnier Wilson stated, " is nothing else but a symptom." There are many conditions which experience has taught are liable to give rise to fits, and to the latter the term *symptomatic epilepsy* is applied ; whereas such fits as apparently occur independently of any known cause are designated *idiopathic epilepsy*. Most patients with the latter type of epilepsy show neither physical nor metabolic abnormality.

A convulsion, as defined by Hughlings Jackson, is " a sudden excessive discharge of many nervous arrangements representing movements at once, or nearly together, because the cells subserving such movements have become highly unstable." The nature of the mechanism or of the altered physio-chemical state of the nerve cells which fires the explosion or excessive discharge remains hypothetical. Electro-encephalography (see p. 1163) demonstrates several abnormal types of rhythm or changes in the electric potential of the brain in different forms of epilepsy. Grey Walter (1938) stated that in about fifty per cent. of epileptics under the age of forty years some aberrance from the normal was present in the electro-encephalogram between attacks. By pneumo-encephalography moderate inequalities in the size of the two lateral ventricles is frequently seen in epileptics, but it is doubtful whether the proportion of abnormality is any greater than in non-epileptics.

Ætiology.—There are certain ages at which convulsions tend to be more common. These are the periods of infancy and puberty. Many of the possible causes of symptomatic convulsions in the early years of life are without influence in this respect in later years. Gowers stated that " three-quarters of the cases of epilepsy begin under twenty years . . . the maximum being at fourteen, fifteen and sixteen. One-eighth of all cases commence during the first three years of life." Speaking of idiopathic epilepsy he also remarked that up to the thirtieth year the number of females affected exceeded that of males. Heredity plays a limited part. Lennox found that the incidence of seizures among near relatives of epileptics was six times greater than in a control group. In regard to " infantile convulsions," Patrick and Levy state that in the after histories

of 752 unselected children about 4 per cent. gave a history of early convulsions, while the figure was 20 per cent. in a group of 500 epileptic patients.

Inciting factors, in the epilepsies, are numerous, and may be vascular, traumatic, neoplastic, inflammatory, toxic and metabolic. The prefix "essential" or "idiopathic" has no meaning beyond signifying the absence of any apparent cause.

During infancy, the susceptibility to "symptomatic" convulsions depends in part on *nervous instability* due to the immature state of the nervous system, which is far from having reached the stage of full structural development. Not only in infants, but even up to the age of eight or ten years, similar morbid conditions excite convulsions in some children but not in others. It is probable that an inherited factor of innate nervous instability exists in the case of the susceptible children. Common inciting causes are of a *toxic* and *febrile* nature, such as acute tonsillitis, otitis media, pneumonia, the exanthemata, and intestinal toxæmia. An indigestible meal in a susceptible child may induce a convulsion, probably acting as a form of reflex irritation.

Metabolic states with which convulsions may be associated are calcium deficiency, as in spasmophilia ; hypoglycæmia from an overdose of insulin ; alkalosis produced by respiratory hyperventilation ; and water-retention in some patients. Convulsions can occur as an expression of allergy, but very rarely do.

Asphyxial convulsions occur in asphyxia neonatorum, congenital laryngeal stridor, breath-holding attacks and whooping-cough.

Cerebral diseases of an inflammatory, traumatic, or neoplastic nature, maldevelopment of the brain, and some forms of intracranial hæmorrhage, are common causes of convulsions whose occurrence may be perpetuated as chronic epilepsy. Symptomatic convulsions occur in hypertensive encephalopathy and in the late stages of hepatic disease.

Emotional disturbance or mal-adjustment is claimed as a possible cause of isolated convulsions, but an innate psychopathic factor is probably always present in addition. A powerful emotional shock may be the stimulus which produces a first fit. Idiopathic epilepsy often originates in this way, but more often develops spontaneously without any apparent relation to an extraneous cause. A neuropathic element in the family history of the epileptic is often obtained, not so much epilepsy itself, but such expressions of instability as hysteria, neurasthenia, migraine, alcoholism, eccentricity, or insanity.

Symptomatology.—The epilepsies in childhood can be divided chronologically into three groups : (A) those which occur at birth and in the neonatal period ; (B) epileptic fits in infancy ; and (C) from the end of the second year onwards.

(A) Eclampsia neonatorum.—Convulsions in the newborn are commonly the result of asphyxia and of intracranial bleeding, especially sub- and extra-dural hæmorrhage (see p. 1242). These conditions are most apt to occur in prolonged and difficult labour, although they may be due to sudden alterations of intracranial pressure as in precipitate delivery, or to vascular immaturity in the premature. Frequent convulsions and

twitchings at birth signify extensive cerebral damage, and the infant seldom survives. A large number of infants who become convulsed soon after birth are found subsequently to be suffering from hemiplegia, bilateral hemiplegia, and amentia.

(B) Epileptic fits in infancy. *Idiopathic convulsions of infancy.*—These sometimes occur in apparently healthy infants, usually males, in the early months of life. At first the fits are infrequent and slight, but their number and severity increases from day to day. This condition was especially described by the late John Thomson. When adequately treated the convulsions are arrested and do not recur, but if not properly controlled the brain may be permanently damaged.

The convulsions of spasmophilia.—Calcium deficiency is a cause of convulsions in the rachitic period between the sixth month and end of the second year. Obvious signs of rickets may be present, or pallor and a flabby atonic state of the muscles may be all that is noticeable. Artificial feeding on a badly adjusted diet with excess of carbohydrate and deficiency of vitamin D is the underlying cause. Estimation of the serum calcium in such cases is commonly between 4 and 8 mgm. per 100 c.cm., in place of the normal 10 to 11 mgm. per cent. Some "teething convulsions" may be of this nature.

Convulsions in cerebral disease.—Towards the end of the first, and throughout the second year of life, convulsions are commonly associated with various forms of non-tuberculous meningitis, post-basic, cerebro-spinal, and suppurative. Twitchings, unilateral and bilateral convulsive movements, in early infancy may be due to congenital syphilis involving the brain and meninges. Amentia is usually present.

The subjects of hydrocephalus, whether congenital or acquired, are sometimes epileptic. Thrombosis of the cerebral sinuses in marasmic infants is an occasional cause of convulsions.

(C) Epileptic fits from the end of the second year onwards.—In the years following infancy convulsions are a common symptom of all forms of suppurative and non-suppurative meningitis and of virus and toxic encephalitis.

Both after and during infancy a favourable type of convulsive tendency is often both *familial and constitutional.* One or other parent or a relative may provide a history of one or more convulsions over several years in childhood without repetition in adult life. One child or more of such parentage may throw a convulsion as an initial symptom of any febrile upset, infectious fevers, tonsillitis, otitis, pneumonia, gastric disturbance, or ascaris infestation. The serum calcium percentages in these cases are normal. Some temporary cortical instability must exist in such cases to allow the common maladies of childhood to be provocative of fits, whereas in other families a concentration of such factors are entirely unproductive of the convulsive element. In a similar group of cases convulsions occur in early childhood during febrile disturbances associated with a marked *ketosis and often vomiting.* The origin of the infection is most commonly tonsillar. The epileptic fits cannot be attributed to the effects of the ketosis, as neither experimentally in animals does acetone,

except in massive dosage, produce convulsions, nor are they a consequence in children of a ketogenic diet.

In some cases of *migraine* in the child, a faint, a fall, less often a convulsion can occur at the height of an attack. The periodic syndrome constituting migraine in the child is composed of headache, commonly frontal and bilateral, abdominal pain, vomiting, and in many cases fever. It is another example of an inherited constitutional tendency implying a nervous instability. There is no causative relationship between migraine and idiopathic epilepsy, although the chronic sufferer from migraine may in later life become subject to epilepsy.

Epilepsy of the idiopathic type may begin at any age. In one-eighth of all cases, as stated by Gowers, the fits begin in the first three years of life. It must be remembered that a small proportion of cases labelled symptomatic in infancy turn out by repetition of the fits in later years to be cases of chronic epilepsy. As a general statement, it is true that symptomatic fits are usually of a generalized type, whilst in idiopathic epilepsy commencing in the early years of life the minor—*petit mal*—rather than the major manifestations are commonest. A qualification of this statement is necessary in regard to fits in cases of amentia, the cerebral diplegias and following encephalitis, in which minor are as common as major attacks. *Petit mal* in an otherwise apparently normal child may be a solitary manifestation of congenital syphilis. In idiopathic epilepsy, stated to have commenced round about puberty, it is surprising in how large a proportion of cases inquiry will elicit a previous history covering several years of unrecognized *petit mal*, referred to by the parents as attacks of vacancy, " turns," " faints," or attributed in the infant to indigestion. The epileptic of normal mentality frequently shows a *periodicity* of fits ; that is, they often occur on going to bed or in the early morning on waking. *Frequency* is variable but is often limited to one or more fits over a day or two at intervals of months. A peculiar little group is shown by some children who have their minor attacks chiefly on sitting down to a meal. It is, generally speaking, commoner for attacks to occur during a state of mental and physical quietude or torpor (bedtime—early morning) than when fully occupied, though in some cases one is told that excitement is provocative of an attack.

Types of fit.—Epileptic phenomena of an elaborate nature are uncommon in children. Psychic fits, ambulatory automatism or *fugue*, hysterical violence and acute temporary mania, rarely occur before puberty.

In *grand mal*, or the major fit, consciousness is lost and the convulsion affects the whole body or one-half before the other and comprises both a tonic and a clonic stage. Vomiting can occur at the start, or follow the attack, when it is associated on recovery of consciousness with headache and a general feeling of exhaustion. Biting of the tongue and evacuation of urine during the paroxysm are less common in children than in adults.

Petit mal, or the minor type, includes many variants from a momentary vacancy with a flicker of the eyelids and facial pallor to twitchings, falling to the ground, minor degrees of automatism, and in infants bending or

salaam attacks. Posturizing attacks with bizarre movements of the arms in young epileptics without total loss of consciousness are usually associated with mental defect.

Jacksonian epilepsy.—In this form the convulsion starts locally and spreads more slowly, or may be restricted to the part at which it originates. The patient may be sensible or slightly dazed, but if the convulsion spreads widely consciousness will be lost. The part affected is usually at the extremity of a limb ; the thumb and corner of the mouth may be affected simultaneously, both being closely approximated in their cortical representation. Sensations of pain, or of pins and needles, in the part affected may precede, accompany, or compose the entire attack.

In childhood, Jacksonian epilepsy is much more often a temporary variant of the idiopathic epileptic tendency, which after a few months will be expressed by some other form of fit, than a signal of a local cerebral lesion, vascular or neoplastic. The limb predominantly affected in local epilepsy may remain paralysed for a considerable period following an attack, which condition is sometimes referred to as Todd's paralysis.

The *epileptic aura* can be psychical, sensory, or motor, and occurs in about half of all cases. Auras in children are absent or simple, the commonest being an abdominal sensation often with audible borborygmi due to sudden irregular peristalsis. Many mothers are convinced that this " gastric trouble " governs the trances, faints or vacancies. A cry as of pain or appearance of fright is next commonest and again suggests a bodily cause to the parent. The complicated hallucinatory visual and auditory auras are reserved, though not exclusively, for the more complex psychic development of the adult. The *uncinate* attacks with olfactory and gustatory sensations are rare in children. In the latter type the child may smack his lips and meanwhile look dazed. In such a case an attack was invariably produced by sucking a boiled sweet, thereby constituting an example of *reflex* epilepsy in which the paroxysm is excited by some stereotyped form of external stimulation.

Epilepsia partialis continua is the name applied to the persistence of local convulsive movements for days on end. In children it appears to occur in the chronic epileptic during a period when major attacks are frequent. It is probably only a minor form of the grouped attacks or *serial* epilepsy when for weeks or months on end, despite all treatment, the daily number of attacks is considerable but with consciousness being almost or fully regained in the intervals.

In *status epilepticus* without any known causation one fit falls upon another so quickly that consciousness between attacks is not regained. The temperature mounts and signs of cardiac failure become ominous. Death may occur if the seizures are not arrested, or later as a result of cardiac failure. No gross changes are found after death, except venous congestion of the brain and marked fatty degeneration of the heart muscle. Such attacks, when survived, are usually not repeated.

Pyknolepsy is an unfortunate term applied to a grouping of minimal attacks of *petit mal* type even up to hundreds a day in children between the ages of four and ten years roughly, in which the response to drugs

is negligible, but in which it was said a spontaneous arrest of attacks and a good prognosis could be expected. The attacks are in no way dissimilar to those of minor epilepsy and major attacks are as liable to occur at a later age as after any other form of minor attack.

Myoclonus-epilepsy of Unverricht.—It is doubtful in what relation to epilepsy the myoclonus-epilepsy of Unverricht stands. It is a familial condition of a progressive nature, usually beginning in later childhood and characterized by epileptic fits, myoclonus, and in the later stages dementia. Degenerative changes have been found in cortical ganglion cells.

The condition may commence in infancy and its victims are commonly of degenerate stock. Direct transmission from one generation to another is exceptional, but a history of epilepsy without myoclonus, or myoclonus without epilepsy, is not unusual among the antecedents.

Lundborg describes three stages in the disease, the first being one of nocturnal epileptic-tetaniform fits. After one or two years the second stage is reached in which myoclonic movements, now in one group of muscles, now in another, occur in the daytime. The more severe myoclonic spasm may pass into an epileptic seizure. In some cases myoclonus and epilepsy appear synchronously. About this time mental deterioration is apparent. In the third stage, the epileptic attacks become rarer, myoclonus more constant, and the patient becomes emaciated and ultimately bedridden. The course of the disease is variable and death may not occur until some ten or twenty years from the onset of symptoms.

Prognosis in the epilepsies.—The immediate prognosis as far as a convulsion is concerned is good. Even newly-born infants rarely die in a first attack. The ultimate prognosis depends upon the cause. Symptomatic convulsions may be a terminal symptom as in hepatic disease, or call attention to a remediable metabolic disturbance as in spasmophilia. In "genuine" epilepsy, unfavourable cases are those with subnormal mentality. Both the mental defect and the epilepsy are signs of an inferiority of cerebral development probably of antenatal origin.

Brighter prospects are possible for the child of normal intelligence subject to epilepsy whatever the type. The longer the spacing between fits accomplished by therapy, the greater is the chance of the threshold of explosiveness being raised. With a prolonged history of minor epilepsy in early childhood, disappearance of the convulsive tendency is unlikely. Provided fits are not frequent and show a periodicity with a morning or evening incidence, then there is a hope that spontaneously or under therapy the convulsive tendency may disappear or be greatly diminished.

Treatment.—In the treatment of *symptomatic* convulsions the primary disorder receives chief consideration. In the "idiopathic convulsions of infancy" chloral is given in repeated small doses, sufficient to render the infant drowsy but still able to suck. At first a dose of one or two grains corresponding to the age of the infants in months is given every two or three hours until the convulsions have ceased. The effects of the drug require to be carefully watched. When the convulsions are due to a calcium deficiency 5 to 10 c.cm. of a 10 per cent. solution of

calcium gluconate, is given intramuscularly or intravenously, vitamin D concentrate by mouth, and in winter ultra-violet radiation.

For *idiopathic* epilepsy a barbiturate is the drug of selection at all ages. The optimum drug and its dosage can only be arrived at by trial and effect, as individual cases of the same age vary greatly in their response to similar dosage. Phenobarbitone (luminal) is the most widely used : in the infant $\frac{1}{8}$ grain three times a day or $\frac{1}{4}$ grain twice daily. Nulepsi, a combination with other antispasmodics in pill form, is sometimes very effective in children over four years, one to three pills a day for a child of eight to ten years. The anticonvulsant soluble phenytoin (epanutin) in $1\frac{1}{2}$-grain doses, one to four a day, is unfortunate as the optimum dosage approaches the toxic level, so that it is to be prescribed only under the closest supervision. Daily combinations of phenytoin and a barbiturate have not given good results. Bromides are depressing, and are now seldom used.

Petit mal with a " wave and spike " type of encephalographic tracing may respond dramatically to troxidone (tridione), but an allergy to the drug occurs in many children, with a severe agranulocytosis, and deaths from its use have been reported. Periodic white cell counts may be necessary, and with a marked fall or the appearance of petechiæ in the skin the drug must be stopped at once. Other measures worthy of trial in *petit mal* are the ketogenic diet (Keith, 1947), and glutamic acid, 2 to 8 gm. thrice daily, sufficient to maintain the *p*H of the urine at about 5·0. In the group of cases in which children have minor attacks at mealtimes chiefly, ephedrine $\frac{1}{2}$ grain before meals is sometimes effective.

Spacing of the drug administration to precede the habitual fit periodicity is important. The aim is not to saturate the patient but to give an adequate dose one hour or so beforehand. Thus the nocturnal epileptic is best suited by a main or single dose at bedtime. Regularity of administration over long periods is essential. Transference from one form of drug to another must be effected gradually in a dovetailed manner of dosage, otherwise an exacerbation of fits may be expected. In cases of serial epilepsy of major and minor type usually in children with some degree of mental inferiority, drugs are often without influence upon the frequency of the fits and all the physician can prognosticate is that in a matter of several weeks, or one to two months, a change over to a different rhythm of the convulsant tendency with fewer fits will occur. Syrup of potassium bromide and pilocarpine is sometimes useful in checking a temporary increase of fits ; 60 to 240 minims may be given daily to a child of three to seven years.

In status epilepticus, sedatives administered rectally are usually expelled owing to intestinal peristalsis taking part in the convulsive hyperaction. An effective and simple method is light chloroform anæsthesia, after which intramuscular paraldehyde, 60 to 120 minims is usually effective. Soluble phenobarbitone subcutaneously or intravenously in 2-grain doses is a useful measure, or bromethol 0·07 to 0·1 c.cm. per kgm. of body-weight given rectally as a 2·5 per cent. solution the effects of which last longer than those of chloroform. In the absence of cardiac

weakness morphine $\frac{1}{40}$ to $\frac{1}{16}$ grain in infants between six months and two years can be used.

The *ketogenic diet* introduced by Wilder and Peterman was extensively used in the treatment of epilepsy, but is seldom now, although occasional cases do respond to it remarkably well. It was claimed by its exponents that roughly 31 per cent. of epileptic children were freed from their attacks and that the number of fits was diminished in another 23 per cent. An effect of this low carbohydrate–high fat diet appears to be a reduction in the water retention of the tissues and a shift towards acidosis, which may in cerebral cells help to reduce the convulsive tendency.

The dietary ratios of grammes fat to carbohydrate are altered gradually from F 1·5–C 1 ; 2–1 ; 2·5–1. If the child is of normal height and weight for its age, its caloric needs are obtained from a table of requirements (Talbot). To obtain kgm. from pounds, divide the number of pounds by 2·2. The number of grammes protein allowed equals the number of kilos body-weight plus 50 per cent. As each gramme protein is the equivalent of 4 calories, the total grammes protein multiplied by four is deducted from the total caloric requirement. The remainder is to be divided between fat and carbohydrate ; for example, at a ratio of F 2 to C 1, then

2 F (9 calories)	= 18
1 C (4 calories)	= 4
	22

The caloric total minus calories derived from grammes protein is divided by 22 : the resulting figure gives the requirements of grammes carbohydrate and is doubled for grammes fat, a ratio of 2 : 1. Suitable foodstuffs in the requisite quantity of grammes C, P and F are selected from a reliable table of food values. Vitamins and the mineral requirements of the growing child must be remembered. Before putting a child on a ketogenic diet it is necessary to make sure that the dietary regime will be rigidly kept. Cases of epilepsy with mental impairment are unsuitable for this form of treatment. Small doses of luminal may be given in conjunction with the ketogenic diet.

General measures.—Apart from the ketogenic diet, foods should be simple, and there is nothing to be gained on *exclusion diets*. The bowels must be kept regular, as constipation is a common symptom in chronic epilepsy. An essential of treatment when possible is for the child to lead as fully active and normal a mental and physical life as possible. He can work for examinations, play games and learn to swim under supervision.

The epileptic colonies, with their system of occupational routine and regularity of meals, are well suited for the ordinary chronic epileptic whose physical strength is sufficient and whose mental calibre is under average.

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13. *NARCOLEPSY*

Narcolepsy is a functional disorder of the nervous system, which in its clinical manifestations is apt to be confused with epilepsy. But the opinion is now generally held that the condition is in no way related either to epilepsy or to hysteria.

Idiopathic narcolepsy is characterized by attacks of irrepressible sleep and by other attacks induced by emotional stimuli, most commonly laughing, in which the patient loses the power of his limbs and sinks to the ground—cataplexy—retaining consciousness of all that goes on around him. In some cases the attacks of sleep are present alone. Males are more often affected than females, and the condition seldom commences before puberty. Weech, however, records a case in a coloured child, a girl, of eight years. These patients are normal in all other aspects and a neurotic inheritance does not seem to be a necessary ætiological factor.

The cataleptic component of narcolepsy, according to Kinnier Wilson, is produced by inhibition of the cortex as a result of emotionally charged impulses reaching it from the thalamus. The inhibition can only be local and not universal as the patient loses the power of movement but retains consciousness.

Symptomatic narcolepsy may have all the clinical features of the idiopathic form, and in association with obesity has been known to follow as an after-effect of epidemic encephalitis, and may also occur in diseases of the pituitary.

For the **treatment** of narcolepsy, ephedrine hydrochloride ½ grain twice a day, has been recommended.

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14. *ELECTRO-ENCEPHALOGRAPHY*

Physiology.—Electrical activity, an aspect of the life of all cells, is particularly evident in excitable tissue such as the nerve cell. In 1875 an Englishman, Caton, observed small currents from the cortex of rabbits. More than fifty years later, in 1929, Berger reported similar waves from the brain of man. By 1934 he had shown that the human brain has an electrical beat, dependent on neurone function, which changes with age, sensory stimulation and the physiochemical state of the body. The most obvious component of this beat is usually a 10 per second rhythm (in adults) and was called " Berger " and later " alpha " rhythm. Another component appearing from the background of potential changes is a faster rhythm, variable in frequency from 18 to over 30 c. per second and called " beta " rhythm. These two rhythms are similar, but with slight frequency differences, to those previously described in animals. The rhythms of the " EEG " (electro-encephalogram) are *spontaneous* fluctuations of potential and are not *evoked* by stimulation of

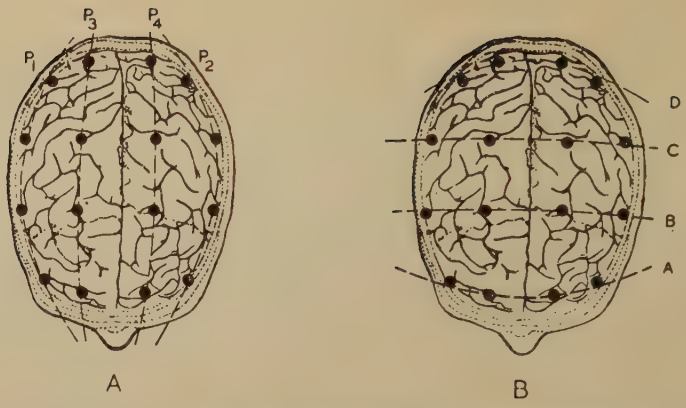


FIG. 332*a*.—STANDARD ELECTRODE POSITIONS. FOUR ANTERO-POSTERIOR LINES OF FOUR ELECTRODES EACH, WHICH CAN BE USED FOR EITHER A.P. (A), OR TRANSVERSE (B) RECORDINGS.

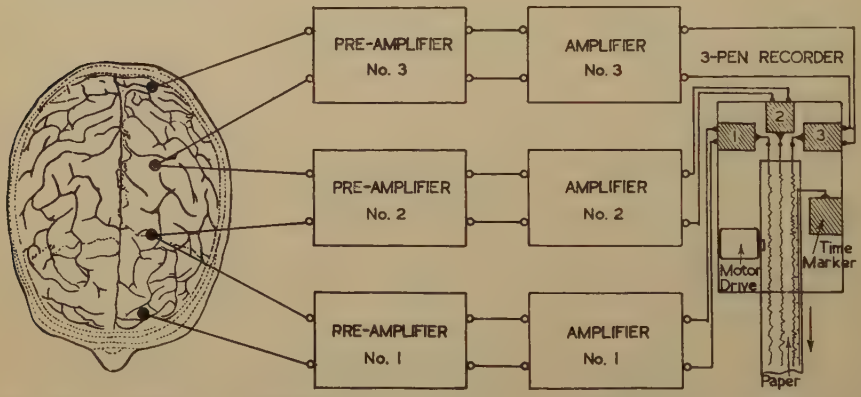


FIG. 332*b*.—SCHEMATIC REPRESENTATION OF 3-CHANNEL EEG APPARATUS, SHOWING INPUT CONNECTIONS FOR THE BIPOLAR TECHNIQUE.

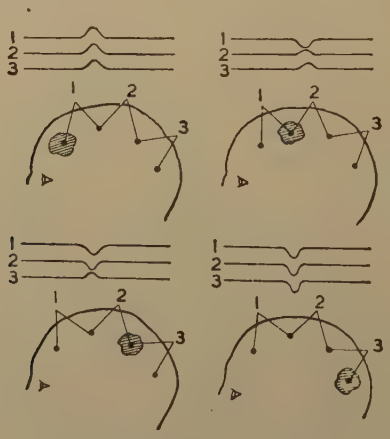


FIG. 332*c*.—LOCATION OF FOCUS.

sensory receptors. They are phenomena of the cortex at rest and are largest when the sensory influx is minimal. They are probably a characteristic of any large number of neurones in isolation. It is at present uncertain whether these slow potentials are compounded of the aggregate *action* potentials of discharging neurones, or whether they are derived from synchronized polarization and depolarization of the membranes of cell-bodies. The spread, localization and frequency of cortical rhythms gives an indication of cerebral function; it is therefore necessary to observe them simultaneously from different areas of the head. For this reason the electro-encephalographic apparatus consists of three or more identical channels of amplification for recording from a similar number of scalp leads. Since location of potentials is important, the separate channels are connected by common electrodes. Fig. 332 *a*, *b*, *c* illustrates a standard technique in common use (bipolar electrodes).

Alpha rhythm is normally the dominant rhythm of the adult EEG. Variability of frequency from individual to individual is from 8 to 13 c. per second and the frequency is constant once sexual maturity has been reached. In the child it appears at any early age, always by the fourth year but may not be dominant before the ninth year. There is great variability in the percentage time occupied by alpha rhythm, in some being present in over 90 per cent. of the record and in others in less than 10 per cent. These differences may be related to differences of habitual imagery. In most children aged nine to ten years it is markedly dominant and of high voltage (75–100 microvolts). The alpha rhythm is intimately associated with the functions of the central visual mechanism. It has been located to the parieto-occipital area in both hemispheres, in each of which it appears equally and more or less synchronously. Its presence is evidence of physiological rest in the visual cortex, and it is normally inhibited by pattern vision and visual thinking. Normal alpha rhythm is not seen in the frontal areas; the rare case in which it is clearly located in a frontal lobe has been usually found to be pathological.

Beta rhythm is less constantly seen than alpha rhythm. It is of lower voltage (10–20 microvolts) and higher frequency (18–30 c. per second). Its occurrence is infrequent in young children. It is found in the precentral regions, is unaffected by visual stimulation or mental effort and is thought to be related to the functions of the sensori-motor cortex. being sometimes inhibited by tactual stimulation. A gross excess of beta rhythm in young children suggests a diffuse organic process.

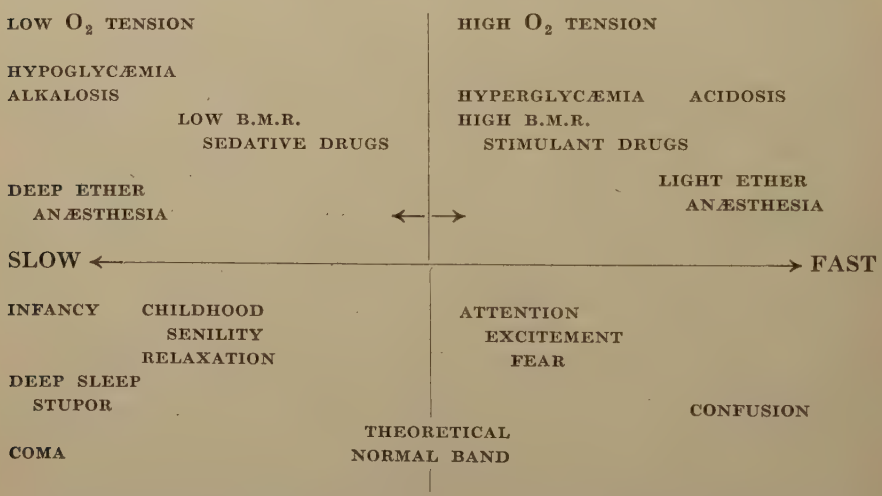
The terms "delta rhythm" and "theta rhythm" have been given to slower frequencies which occur normally in early life as well as in sleep and certain pathological states at any age.

Delta rhythm is a normal characteristic of the EEG during the first months of life and later in deep sleep. The frequency range is from $\frac{1}{2}$ to 3 c. per second. In pathological states it is usually of high voltage and when present persistently in all areas is associated with unconsciousness or with severe impairment of mental functions.

Theta rhythm is the term given by Walter to the frequency band 4 to 7 c. per second and is commonly found in young children. The rhythm

is seen to a certain extent up to the sixteenth year and is then usually central and temporal in distribution, bilaterally synchronous with a voltage approximating to that of the alpha rhythm. Theta rhythm in excess is the characteristic abnormality among behaviour problem children, but can follow encephalitis, disease or damage of basal grey matter.

Although the chief rhythms remain, under constant conditions, an unchanging characteristic of the individual from maturity to the senile period, the distribution of activity at different frequencies changes with variations of the physical and chemical environment. Thus excitement, attention, mental activity and anxiety increase the activity in the fast frequencies. Whilst anoxæmia, hypoglycæmia and alkalosis shift the activity towards the slow frequencies, hyperglycæmia and acidosis shift it towards the fast, though less obviously. The effect of the central stimulants caffeine and amphetamine (shift to fast frequencies) are contrasted in the EEG by the depressants morphine and the barbiturates (shift to slow frequencies). These observations have been made upon adults, but there is every reason to believe that the child's brain behaves in a similar manner. Using data from many sources it is possible to show in diagrammatic form the influence of psychological and physiological factors upon the EEG.



Fortunately for EEG interpretation these factors, with the exception of age and blood sugar level, are rarely present sufficiently to impair interpretation of the record. A high concentration of sugar in the blood may mask abnormalities present when the patient is starving, and it is therefore usual to examine patients not less than four hours after a meal.

Ontogenesis.—One of the chief difficulties of interpretation of the EEG in children is that throughout childhood the characters of the cortical rhythms are changing. Much research will be necessary before a "normal" can be described for any given age. Only the broad outlines are discernible. Very little rhythmical activity is apparent in the

EEG of the waking neonate, but by the sixth to seventh month two rhythms are apparent—one in the central regions, another in the occipital regions. The rhythm of the occipital regions increases in frequency from 3–4 c. per second to the alpha frequency according to an exponential curve which flattens out by the tenth to the thirteenth year. The central rhythm also increases in frequency and by the fifth year is usually at 5–6 c. per second and of large amplitude, dominating most areas of the cortex (theta rhythm). After this period there is a progressive decline in the amplitude of the central theta rhythm and a progressive increase in the amplitude of the occipital alpha rhythm, which, as already indicated, is still increasing in frequency. By the ninth year the majority have a high amplitude rhythm in the occipital areas of alpha frequency, while the frontal and parietal areas lag behind with a persistence of slower waves. From nine until eighteen years further changes occur in the EEG which during these years acquires the characters which give it individuality. Thus the low voltage fast alpha type of EEG is rarely seen before the age of fourteen years. The years twelve to fifteen are noted for the common occurrence of diffuse theta rhythm (4–7 c. per second) of low voltage in the parietal areas. The important field of ontogenesis is likely to remain obscure for some time owing to the extreme inter-individual variability. Automatic frequency analysis offers the best method at present for clarifying the general picture and some preliminary results, using the Walter apparatus, have been reported by him. This work emphasizes the importance of the masking effect of low frequency rhythms on higher frequency " normal " ones in children's EEGs. It suggests that the adult frequencies are present even in the young infant's brain but are not seen on visual inspection because of the " dominance " of slower waves. Walter also found evidence of several sudden jumps in development, the suggestion of wavering of hemisphere dominance and on the basis of the view that theta rhythm is an expression of subcortical activity, of dominance of such activity in younger children.

Pathology. Heredity.—Twin studies show that the general characters of the cortical rhythms are congenitally determined. Lennox, Gibbs and Gibbs (Harvard studies) examined 70 twins ; of 53 without evidence of brain injury, the records of monozygotic pairs were indistinguishable in 87 per cent., and in only 4 per cent. was there no similarity. This was not the case in the dizygotic twins. But though it is evident that the EEG characters are genetically determined, it is clear that they are an aspect of constitution which is readily changeable, either temporarily or permanently, by any alteration of cerebral metabolism. The Harvard workers also claim that the *predisposition* to epilepsy is a hereditary " cerebral dysrhythmia." Five pairs of identical twins were studied. In one pair both twins, and in the others, one twin had seizures. In all five, both twins had dysrhythmia, and in each pair there was a similarity of the fundamental rhythms. In a study of 88 epileptics both parents had dysrhythmia in 35 per cent. of cases. In only 5 per cent. did both have unmistakably normal records. Of 280 relatives of epileptics 52 per cent. were judged normal. Persons with

dysrhythmia and a predisposition outnumber actual epileptics by about 25 to 1, and form 12 per cent. of the population. The Harvard studies therefore suggest that if an epileptic marries, his chance of having epileptic offspring will be less if his partner has a normal EEG.

The presence of non-specific dysrhythmia in varying degrees in groups of *behaviour problem children*, psychoneurotics and psychopathic personalities in the absence of cerebral lesions, has suggested that constitutional cerebral dysrhythmia is associated with a predisposition to functional nervous disorders other than epilepsy. It is of interest that Gottlieb, Ashby and Knott (1947) found a significant number of abnormal EEGs among the parents of behaviour problem children whose EEGs were abnormal. However, some cerebral lesions in early life can produce the same type of non-specific dysrhythmia as that found in these groups. In the absence of a clearly defined single focus of abnormal potentials—very rarely seen in these cases—there are no characters in the EEG which will distinguish what is acquired from what is laid down by heredity.

Location of abnormal function.—Cortical potentials are an expression of cortical function. Tumour tissue, atrophic cortex, traumatic or other cysts are themselves electrically inert, the potentials by which they can be located arising from neighbouring tissue, the function of which is disturbed. Chronic pathological processes in which the functional interference with normal brain tissue is minimal may not therefore give rise to abnormal potentials. By contrast, rapidly developing lesions and toxic processes interfere with cerebral function over a wide area, and the electrical disturbance is equally widespread. Raised intracranial pressure associated with block in the ventricular system results in delta-wave discharge from all areas.

The two methods in common use for the location of cortical potentials are known as the unipolar and bipolar techniques. In the former, an "indifferent" electrode is connected to the ear lobe to be far from the active cortex and an "active" electrode placed near to the suspected lesion. When multiple separate channels of amplification are used, the "indifferent" electrodes are all connected to the ear lobes and the "active" electrodes spread out on the same side of the cranium according to a standard plan (Jasper). By this method the focus is located nearest to the "active" electrode from which the abnormal potentials have the greatest voltage. The nearer the "active" electrode can be placed to the source of activity, the greater the voltage of the potentials and the better the location.

The bipolar technique, originally used by Adrian to locate the alpha focus, and by Walter to locate cerebral tumours, is the method of choice in England. The most accurate location of surface cortical potentials may be obtained by this method. Since all electrodes are "active," *i.e.*, equally near to cortex, they are arranged in lines either antero-posteriorly or transversely across the head and use is made of the phase relations of potentials in the various channels. The latter are connected in such a way that a source of potentials beneath an electrode common to two channels produces out-of-phase deflections in those two channels,

and in such a case the electrode can be said to be over the source. By the bipolar method, as in the unipolar, the voltage of the potentials is determined not only by the activity of the source and the resistance of the supporting tissues, but also by the distance between the electrodes.

Specificity of wave-form and focus. (*a*) *Epileptic wave-forms.*—The Harvard workers identified specific wave-forms for *petit mal* (3 c. per second alternating wave and spike), *grand mal* (paroxysmal fast) and psychomotor epilepsy (square-topped high voltage 4 c. per second). When one of these is found in an EEG they claimed that the patient suffers from the corresponding type of fit. The specificity of these wave-forms has, however, been questioned (McGill studies) since wave and spike complexes are frequently seen in epileptics who have only *grand mal*, and paroxysmal fast frequencies in other epileptics who have never had a major convulsion. There is no doubt, however, that during a *petit mal* fit, the wave and spike discharge is the constant accompaniment. The Harvard workers later added a fourth specific epileptic wave-form, the "*petit mal* variant"—a slow spike and wave or "sharp" wave, but these wave-forms are found in encephalitics and degenerative disorders as well as in the EEGs of idiopathic epileptics. While the 3 c. per second wave and spike discharge shows greatest specificity, paroxysmal fast frequencies are associated with a variety of clinical patterns. Moreover it is now appreciated that the "square-topped" waves of psychomotor epilepsy are not sine-waves at all, but a series of long duration spikes, equally spaced at 4 to 5 a second. The spikes most frequently have an origin in the anterior part of a temporal lobe.

(*b*) *Other wave-forms and foci.*—Generalized delta waves are related to factors depressing cortical function—chronic degenerative processes of all kinds. On the other hand the local irregular delta wave focus is more frequently associated with localizing clinical signs than any other type, with the possible exception of the "spike" focus. The paroxysmal high voltage delta wave discharge of the young or deteriorated epileptic has a sinusoidal form, in contrast to that due to a rapidly growing neoplasm which is less paroxysmal and more irregular in form. While this difference may be recognized by the electro-encephalographer it is impossible to identify with certainty a neoplastic process by the wave-forms. The latter can only indicate an area of abnormal function, and the same is true for infective, atrophic or traumatic lesions.

Both the McGill and Harvard studies agree that three types of discharge—the focal delta wave, the focal single spike and the focal sharp wave—are more frequently found with local cortical lesions than any others. Jasper, with extensive experience of correlating EEG and surgical findings, relates the focal single spike to superficial epileptogenic lesions and the focal sharp wave to extensive deeper lesions. But in neither case can the pathology be specifically determined from the wave-form. Sharp wave foci are frequently found in the temporal lobes and are commonly bilateral, although the structural lesion, if present, is unilateral and subcortical. Multiple sharp waves, without clear location, are related to diffuse cortical atrophy (McGill studies).

Clinical Studies

Idiopathic epilepsy.—The Harvard studies suggest that cerebral dysrhythmia is an indication of inherited predisposition to this form of epilepsy. The characteristic EEG record shows an alpha rhythm of great variability of frequency and bursts of delta and high voltage beta rhythm. Paroxysmal discharges tend to be bilaterally synchronous, though not invariably. Some show only fast and others only slow frequencies. Whilst the presence of these abnormalities in a child suspected of epileptic phenomena is corroborative evidence, the diagnosis is not confirmed until a "larval" attack is seen in the record. The 3 c. per second wave and spike complexes of *petit mal*, which are the commonest bilaterally synchronous discharge and have the strongest hereditary determinants, are very frequently seen in the EEG of epileptic children (30 per cent.). The *petit mal* variant, provided it is bilaterally synchronous without single location, is again good evidence of "active" epilepsy, but, as already mentioned, is not evidence of its idiopathic nature. The *grand mal* type of discharge is probably less determined by heredity, since it may indicate the onset of a convulsion which is initiated by a spreading discharge from an acquired lesion.

Minor epilepsy (*petit mal*).—The fit is accompanied by a bilaterally synchronous 3 per second alternating wave and spike discharge which can appear from all cortical areas simultaneously or appear briefly in the frontal areas first. Short paroxysms of the discharge ("larval" attacks) are seen consisting of 2 to 6 wave-forms. If the discharge lasts longer than 3 seconds clinical *petit mal* is usually apparent. The type of disorder with which this discharge is associated is a brief loss of consciousness usually without motor activity but if present, the latter consists of a 3 per second rhythmic jerking of the eyelids, head or arms As the fit proceeds the frequency of the waves decreases and the spike component tends to disappear (fig. 333). The discharge is readily induced by periods of hyperpnœa and in many cases can be stopped by a strong sensory stimulus. Brief larval attacks are broken up by opening the eyes and in some patients closure of eyes will repeatedly induce them. Whilst alkalosis induces the attacks, acidosis reduces their frequency. Hypoglycæmia precipitates the discharge but it is doubtful whether hyperglycæmia prevents it. Thirty per cent. of all epileptic children show wave and spike discharge which is more than twice the incidence in epileptic adults. The specificity for idiopathic epilepsy is great and the discharge is not seen in true traumatic epileptics (Walter). The hereditary factor is indicated by the Harvard studies. The discharge was present in 77 per cent. of epileptics with clinical *petit mal* and in only 5·9 per cent. of those without it; it was found in 0·2 per cent. of 3070 controls but was present in 3·5 per cent. of 202 relatives of epileptics.

Pyknolepsy.—The pyknoleptic discharge is in many cases indistinguishable from the *petit mal* discharge described above. The between-seizure dysrhythmia in these cases is frequently characterized by occipital delta wave foci. Paroxysmal outbursts of wave and spike complexes are

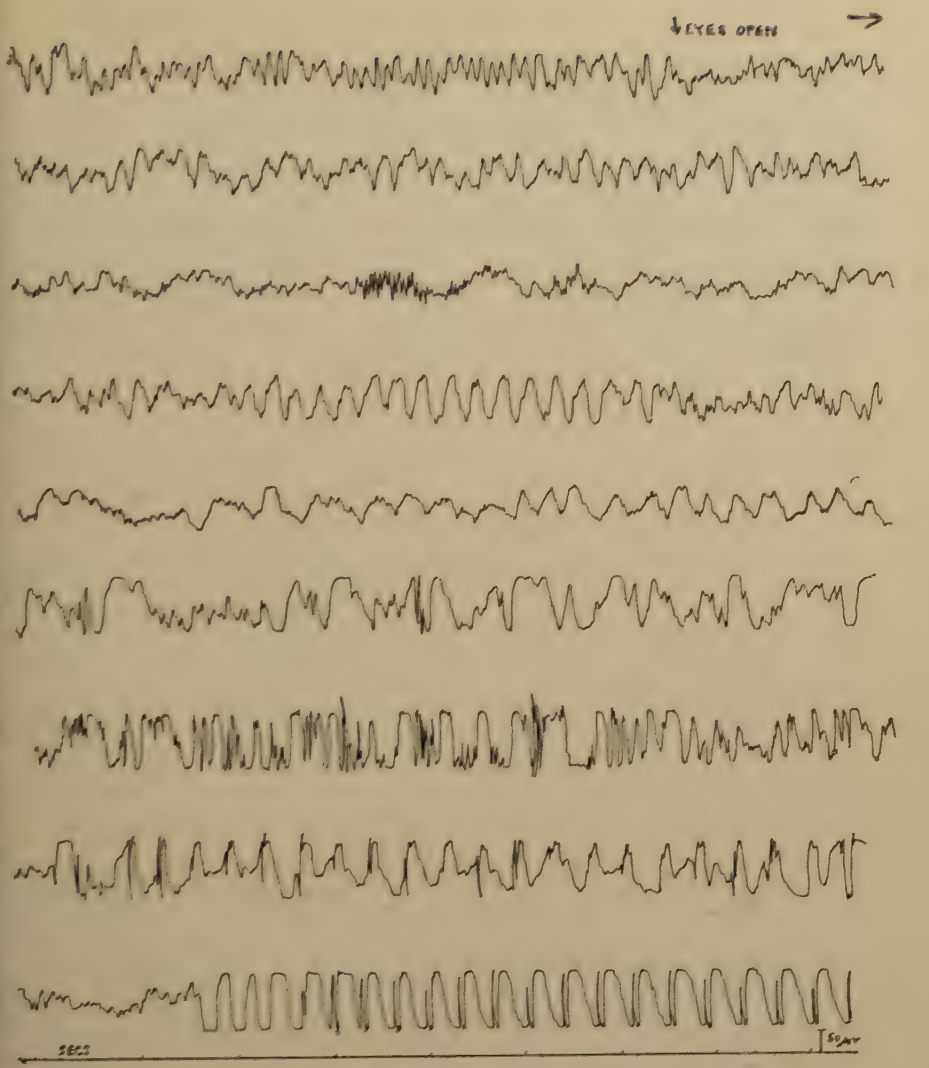


FIG. 333.—EEG RHYTHMS.

(1) Female, aged four years. No fits, alpha rhythm dominant at 9–10 c. per sec.
(2) Female, aged five years. Suspected epilepsy, theta rhythm dominant at 4–5 c. per sec.
(3) Male, aged six years. Epileptic. Burst of beta rhythm at 18–20 c. per sec.
(4) Male, aged six years. Epileptic. Burst of delta rhythm at 3–4 c. per sec.
(5) Female, aged 15 years. Recovery from head injury. Generalized delta rhythm at 3 c. per sec.
(6) Female, aged seven years. Myoclonic epilepsy. Random spikes and slow delta rhythm.
(7) Male, aged eight years. Epileptic. Irregular spike and slow wave discharge with altered consciousness.
(8) Male, aged eight years. *Petit mal*. Spike and wave with associated jerking of head and arms.
(9) Female, aged eight years. *Petit mal*. 3 per sec. alternating wave and spike. Loss of consciousness; no movements.

In the last four records, the squaring of the tops of many of the waves is due to overloading the apparatus by the very great increase in size of the potentials during the paroxysms.

seen very frequently in these cases and in a small number appear whenever the eyes are closed. Occasionally it is possible to demonstrate the first appearance of the discharge in the occipital areas.

Major epilepsy (*grand mal*).—When major convulsions occur without evidence of focal cortical onset, the resting dysrhythmia has the (bimodal) characters described above, although fast frequencies are less commonly seen than in adults. The *grand mal* larval attacks consist of a crescendo burst of fast frequencies (over 14 c. per second) seen usually in the precentral areas. If a convulsion follows, the amplitude of the crescendo falls and then increases again during the tonic stage. With the onset of clonus slow high voltage delta waves dominate the record and are synchronous with the clonus. The fast activity is seen superimposed on the crests of the delta waves. As the clonus ends the voltage of the delta waves decreases. During the early stages of stupor there may be an absence of cortical activity, to be replaced as the stupor lightens by delta and finally alpha rhythm. In status epilepticus, the cycle of events is repeated without recovery from the delta activity of stupor. Although idiopathic *grand mal* alone, without *petit mal*, is less frequent in children than in adults, the incidence of crescendo fast frequencies in the EEG of all epileptic children is commoner than in epileptic adults.

Myoclonic epilepsy.—Myoclonia, local or general, some forms of which have a hereditary tendency, is associated with cortical spike discharges. Numerous short bursts of subclinical wave and spike, multiple spikes and delta activity are also described. The correlation of local myoclonia with local spike discharge in the expected area is not good.

Psychomotor epilepsy.—The form of epilepsy in which violent, excited, aggressive or destructive behaviour or fugue states with wandering and apparently purposive activity is associated with amnesia, but without generalized convulsions, is associated with a discharge of bilateral 6 c. per second activity which gradually increases in voltage and declines in frequency to reach 3 to 2 c. per second when the discharge ceases, to leave the record arrhythmic for a varying period. At times spikes are associated. During this discharge, which may last from 80 to 120 seconds or so, the patient is relatively motionless ; thereafter during the period of arrhythmia—a post-ictal paralysis, the " automatic " behaviour occurs. Unconsciousness is profound during the period of the discharge, and is gradually recovered during the post-ictal phase. This may take as long as twenty minutes. In a second type the discharge described above is confined to one hemisphere and some hold on consciousness is retained so that subsequently the patient may describe a " dream state," hallucinations, bizarre experiences and the like. Recovery from this state is rapid both clinically and in the EEG. The focal EEG disturbance which is usually of " sharp " waves, *i.e.* slow spikes, is located either on the surface of, or beneath, a temporal lobe. Psychomotor attacks as the only manifestation of epilepsy are rare in children and the seizure pattern is less frequently seen in them than in adults.

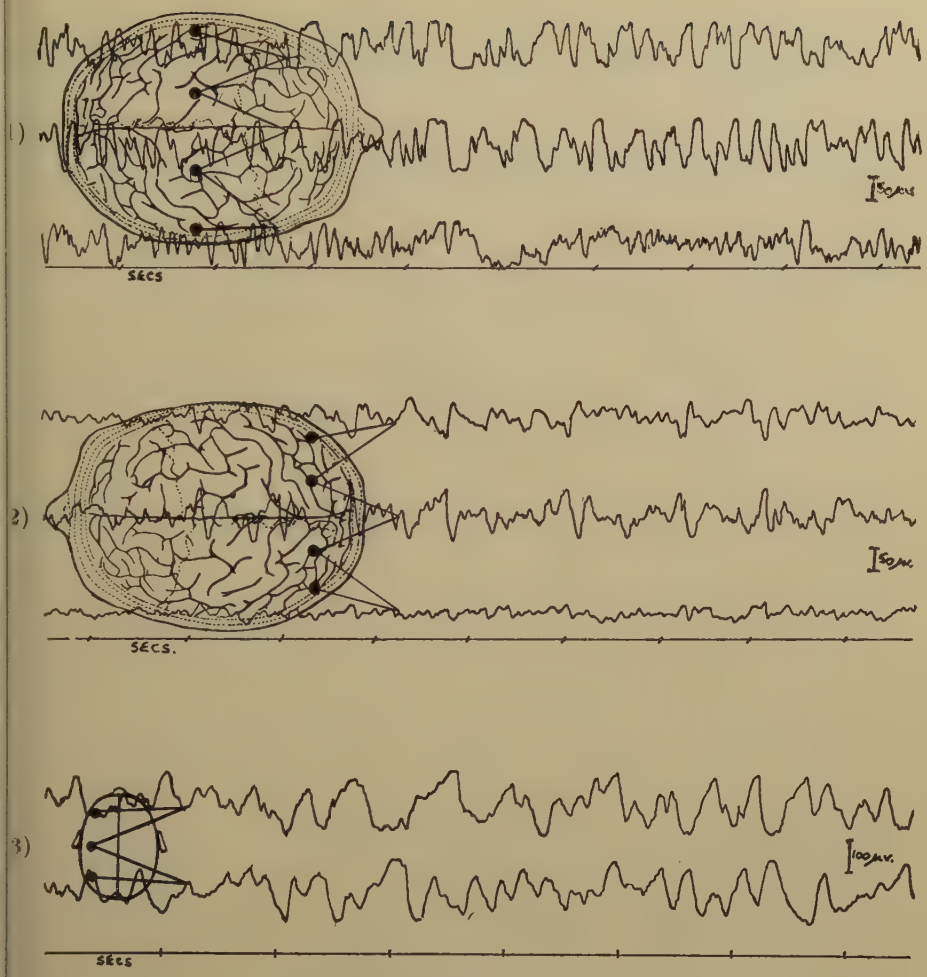


FIG. 334.—CEREBRAL LOCATION.

(1) Female, aged sixteen years. Focus of theta and delta waves located to left central region, over a wide area. Frequent severe fits with right-sided onset; right facial weakness. Pneumo-encephalogram showed ventricle in left premotor region drawn up into a sharp spike. At operation hard scar found deep to the left motor area.

(2) Male, aged fourteen years. Focus of sharp waves and low voltage spike potentials, located to the right post-parietal region. Epileptic since infancy. Major fits preceded by pain in the left hand travelling up the arm which is then drawn up. Head and eyes turn to the left.

(3) Female, aged twelve years. Focus of delta waves located to the left hemisphere, chiefly in the parietal region. Some generalized irregular slow rhythms due to high pressure. Operation: Left parieto-temporal astrocytoma of large size.

(Kindly lent by Dr. W. Cobb.)

Symptomatic epilepsy (*acquired, focal, cortical*). –The presence of a well-defined focus of abnormal potentials of any type, in the absence of a generalized or bilaterally synchronous dysrhythmia, always suggests the possibility of a local cerebral lesion. Local delta wave, local sharp wave and local spike are particularly related to cortical lesions, and the last two with epileptogenic lesions. EEG foci are very common in children with traumatic epilepsy (67 per cent.) and among all epileptics clinical evidence of localized damage to the brain was present in only 1 per cent. of those without an EEG focus, and in 58 per cent. with one (Harvard studies). The foci localized were corroborative in 87 per cent. of 106 cases with clinical localizing signs.

The EEG, however, as already stated, can only indicate the type and the extensiveness of the lesion although asymmetry of the basic rhythms in the two hemispheres, where an abnormal focus is present on one side, strongly suggests a widely spread lesion.

The value of hyperpnœa.—Alkalosis, induced by two to three minutes voluntary hyperpnœa, may induce one of the specific wave-forms of epilepsy (usually the alternating wave and spike) and for this reason the procedure has become routine. Some importance has been placed in the past upon a discharge of delta rhythm but since it occurs in over 40 per cent. of normal children, and the percentage is higher in the fasting state, the rhythm produced in this manner has no significance in the diagnosis of epilepsy in children. The stress of alkalosis may demonstrate dramatically an impairment of function in one hemisphere from a birth injury or atrophic lesion, when the opposite side is unaffected. It is frequently found that the rhythms on the damaged side remain unaffected by hyperpnœa, while those on the normal side show the usual change to delta waves. This is the opposite effect to that seen in the injured brain of the adult, in which the side of the lesion tends to show instability on hyperpnœa.

Epilepsy with deterioration.—Epileptic children with severe mental deterioration rarely have a normal EEG. Usually the dominant rhythm is in the theta band (5 to 7 c. per second) and little alpha rhythm, if any, is present. Characteristically, arousal stimuli fail to inhibit the wave whether they be at theta or alpha frequency. Diffuse slow irregular delta rhythm is also evident in most cases.

Cerebral tumour.—Since most tumours in children are subtentorial it is unfortunate that the EEG is of very little value in the location of cerebellar lesions. Walter reports that theta rhythm, usually present, may have a lateralizing value. The results are, however, disappointing, although the absence of a cerebral cortical focus may assist in the diagnosis. More often the EEG shows a gross generalized disturbance associated with the raised pressure in the ventricles. In some cases reduction of cerebral œdema by intravenous 50 per cent. sucrose will temporarily reduce the generalized disturbance leaving a focus of abnormal potentials at the site of the lesion, but the method is unreliable.

Cerebral tumours in the cortex or subcortex, without generalized cerebral œdema, usually present a clear focus of abnormal potentials.

As already indicated the degree of electrical disturbance depends on the extent of dysfunction in brain tissue surrounding the growth, which is itself electrically inactive. Thus the greatest EEG change is found in the most rapidly growing gliomas. In these cases a delta wave focus of high voltage potentials with irregular form is the common finding. Tumours involving the thalamus, or structures in floor and walls of the third ventricle, may give rise to non-focal theta rhythm, on one or both sides, usually in the anterior and lower aspect of the hemisphere.

Whereas a well-defined focus may give a clear indication of the presence of the suspected tumour, its precise location, size and depth can rarely be assessed by means of the EEG. Usually a lobe or adjacent lobes of the brain are identified as the probable site of the lesion. However, recent work suggests that while deep tumours are associated with surface theta rhythm and superficial tumour with delta rhythm, some idea of the depth and size of the lesion can be obtained from the ratio of theta waves to delta waves in the EEG pattern.

Cerebral trauma.—On EEG evidence the child's brain is more susceptible than the adult's to trauma. Abnormalities in the EEG which may last for life and tend to be focal are usual following injuries with a long post-traumatic amnesia. The likelihood of an abnormal EEG persisting after the acute stage depends upon the severity of the injury. Focal abnormality is strongly suggestive of brain damage whereas no significance should be attached to generalized (diffuse) abnormality unless definite asymmetry of the rhythms on the two hemispheres is present. There can be asymmetry of frequency, of amplitude or of distribution of rhythms ; and there may also be an asymmetrical response to arousal stimuli or to hyperpnœa.

Focal abnormalities are commoner in children than in adults following head injury and occur in a high percentage of cases with dural penetration. The EEG can be expected to show improvement over a period of two years in cases uncomplicated by epilepsy and it is clear that in many instances the EEG returns to normal although this does not necessarily mean that the brain has not been permanently damaged. In the recovery stage from severe injury, bilateral paroxysmal delta rhythm is commonly seen which disappears after a few weeks or months. After the third month the EEG has returned to normal in nearly 50 per cent. of cases. Unfortunately post-traumatic epilepsy cannot be predicted by an EEG study during the recovery stage.

Other cerebral disorders.—The development of dysrhythmia with an acute encephalitis with subsequent EEG and clinical recovery, has been observed in a child. But the EEG does not return to normal invariably. Foci of " sharp " waves are not uncommon following local encephalitis and such foci are usually associated with epilepsy. In the rare forms of subacute leuco-encephalitis described by Van Bogaert and Dawson which usually end fatally, five cases of which have been seen by the author (Cobb and Hill), unique and almost specific changes occur in the EEG. In the late stages of the disease bursts of high voltage very slow grouped waves recur every few seconds with a periodic occurrence.

In the intervals between the bursts the record becomes arrhythmic. The bursts are themselves remarkable because of the similarity of the wave forms and the constant phase relationships of the components from one burst to another. The burst activity is found to relate in time to the start of each occasion of involuntary movements which characterize the condition. In meningitis delta wave discharge may be seen, depending on the degree of extension of the inflammatory process into the brain. Cerebral abscess which is cortical or sub-cortical can in most instances be located by the EEG. The demyelinating dementias, of which Schilder's disease has been best studied, produce profound change characterized by slow, high voltage delta rhythm and occasional epileptic discharge. When hydrocephalus is associated with gross neurological disorder the rhythms are usually abnormal but the pattern is by no means constant.

Mental defect.—When mental defect is neither related to gross failure of cerebral development nor to severe lesions at the start of life, no EEG abnormality can be expected. There is no correlation between the EEG characters and mental age above five years (M.A.). In mongoloid imbeciles on the other hand, EEG abnormalities occur and the lower the mental grade the less the alpha activity. Cretins commonly show many abnormal potentials but no correlation between intelligence level and frequency of rhythms is known. Among the group of low grade defectives who excrete phenylpyruvic acid in the urine, there is an alleged association between the amount of alpha rhythm and the mental age.

Behaviour disorders.—A high percentage of children with the severer forms of behaviour disorder but in whom there is no history or clinical evidence of an acquired cerebral lesion, show an abnormal EEG. The dysrhythmia in these cases appears to correlate specially well with hyperkinesis, irritability, temper-tantrums and enuresis. Antisocial behaviour is commonly part of the clinical syndrome, but its presence or absence is not related to abnormality or normality of the EEG. An excess of theta (4 to 7 c. per second) rhythm is the usual finding though occasionally delta rhythm is also seen. The potentials are usually bilaterally synchronous and not of great amplitude. The condition has been termed " epileptoid " by Jasper but there is no evidence from the EEG that epileptic discharge actually occurs in these patients. Theta rhythm is normally seen in the EEG of children and at the present time assessment of an excess is judged on visual appearances. This "excess" of theta rhythm is, however, generally recognized and has led to the concept of " immaturity " in the nervous system in this group. No doubt in many patients the EEG becomes normal in the course of years. Treatment with amphetamine sulphate, which in many cases produces marked clinical improvement, has little immediate effect on the EEG. It does not seem justifiable at present to ascribe the excess theta rhythm in these cases either to unrecognized birth injury, birth anoxia or encephalitis, or to the effects of abnormal genetic factors, such as the epileptic predisposition. The further investigation of this difficult problem may be made easier by the methods of automatic analysis, but

it is clear that the scope of such investigations must be thrown very wide if a partial and incorrect explanation of the phenomena is to be avoided.

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CHAPTER XXVI

CONGENITAL MENTAL DEFECT IN CHILDHOOD

W. G. WYLLIE

MENTAL DEFICIENCY IN CHILDREN: AMENTIA

The diagnosis of mental defect in general

A recognition of the *normal* from birth onwards must precede that of the abnormal states. The greatest advance in the study of intelligence and behaviour of the infant and pre-school child have come from the Bühlers in Vienna and Gesell at Yale University. With a little understanding of what to expect of the infant at different stages, the medical practitioner advising, for instance, on the suitability of an infant for adoption would be less likely to make one of those far too numerous mistakes in which as time passes the defectiveness of the adoptée becomes painfully obvious.

Milestones of development.—Before proceeding to outline the symptoms associated with mental defect, it is as well to mention some of the simple data in the development of the normal child, though no rigid time-table for the appearance of new acquirements can be looked for (see page 83).

The new-born babe should suck vigorously from the first few days. By the third week, the eyes fix bright stationary objects and the head is turned in the direction of a light. It is not until the end of the third month that control of conjugate movements of the eyes is fully acquired. Before this age the infant is often seen to squint.

Efforts to hold up the head are begun at the eighth week, and at the twelfth to sit up. At six months the infant is able to sit up unaided. By the ninth, he can pull himself upright and stand with support. At the end of a year, he makes attempts to walk, and can do so alone by the eighteenth month. By this time, the sphincters are usually under control by day, but nocturnal incontinence of urine continues until the end of the second year.

The infant starts to speak in monosyllabic fashion, "Mum" and "Dad," about the ninth month. Up to the age of five, a child's language largely consists in repeating words, or in uttering his thoughts aloud. In this "egocentric" form of language, the child speaks for the pleasure of hearing his own voice, and most of his statements are made without any desire to have them answered. The child plays quite happily by himself up to the fifth year and does not seek the collaboration of other children. Between the fifth and seventh years, his activities become more "socialized." Argument and reasoning begin to develop, and the child asks the reason "why?"

By the time school age has arrived, a child can be judged in regard to his educational aptitudes by reference to well-recognized standards.

A general estimation of a child's powers of perception, continuity of attention, method of working, whether by chance or according to plan, and the character of his mental associations, can be made by employing one of the group of graduated tasks drawn up for this purpose. The revised tests of Binet and Simon have received the widest acceptance, and are so formulated that a test assigned to a particular age would be passed successfully by over 75 per cent. of children of that age (Terman).

Recognition of mental defect.—The recognition of the presence and of the degree of mental defect in a child must depend on what the physician notices and on facts he ascertains, rather than on any opinions given by his relatives, although these must not be disregarded.

In investigating the intelligence of boys and girls of school age, it is natural to proceed by questioning their parents as to the usual indications of mental capacity present. We ask how the children behave, and if in nursery and family life they show ordinary common sense and propriety, and get on well with their fellows. We also wish to know if they can be trusted to do an errand, and if they can carry more than one message in their heads at a time. We inquire how they have done such lessons as they have had, and if they can recognize and copy letters of the alphabet, numerals and pictures, can count, repeat nursery rhymes, and so on.

In children of all ages, in addition to obtaining some insight into the state of the child's intelligence from what the parents tell us, we meanwhile form impressions from our observations of the child before us, and seek by pertinent questioning any points in the past history which may bear upon the present state. Any peculiarities of bodily conformation, movement, gesture, or behaviour at once attract attention.

Certain abnormalities of bodily conformation.—Mental defect of some degree is a usual accompaniment of microcephaly, mongolism gargoylism, cerebral diplegia, severe grades of hydrocephalus, and of cretinism. The recognition of any one of these conditions with few exceptions implies a diagnosis of amentia.

Minor bodily malformations, such as hare-lip, abnormally vaulted, or cleft palate, deformed or asymmetrical ears, marked epicanthic folds, spina bifida occulta, congenital malformations of the heart and other congenital abnormalities, are in themselves no proof of mental deficiency, for all of them are often met with in children of perfectly normal intellect. When, however, several of them are found together, they may be looked upon as providing some confirmatory evidence in doubtful cases.

Abnormal gestures.—In many cases, the child's want of intellect is at once obvious from his abnormal gestures and actions. In early infancy there may be continual senseless crying and fretfulness, which is apt to be attributed to all sorts of supposed internal pains and discomforts before the real cause is suspected. A grave indication of arrested intelligence is a state of utter apathy to surrounding circumstances, with absence of the normal reflex muscular movements. In older children, the restless and the impassive types are also noticed. There may be continuous restlessness, where the attention cannot be held, unmeaning laughter and crying, indistinct speech, exaggerated gestures,

wayward and impulsive actions, and possibly dirty habits and unclean ways of eating food. Continual dribbling of saliva is a common occurrence in mentally defective children, whilst grinding of the teeth in waking hours is seldom met with except in severe cases of amentia. In other children, mental defect may be suggested by a lack of interest in surroundings, mental torpidity, and bodily inertia with a tendency to obesity.

FIG. 335.—CRETIN (TREATED) AGED TWENTY-FIVE YEARS.

DELAY IN THE DEVELOPMENT OF THE BODILY AND MENTAL POWERS.—In many cases of amentia, the first sign that anything is wrong is to be found in the child's being far too long in gaining a proper control over his voluntary muscles and the use of his special senses. Thus, defect should be thought of when a baby, without obvious cause, is backward in learning to hold up the head, to grasp things, to sit, stand or walk. It is also a particularly bad sign if any infant whose body seems normal does not show the natural craving of the healthy child to be constantly exercising all his growing faculties. It has a similar significance when a baby whose sight and hearing are normal shows no interest in bright and moving objects, is backward in responding to the smile, the voice, and the touch of his mother, or nurse, and, at a later age, in beginning to speak. Undue delay in acquiring the usual control over the action of the bladder and bowel is another circumstance which may add to suspicions as to the state of the intelligence.

Backwardness in the acquisition of normal actions often, of course, depends on the temporary weakness which accompanies and follows exhausting disease. If, however, it is present in a marked degree, without any evident debility to account for it, we shall probably be right in suspecting mental deficiency.

It is sometimes no easy matter to distinguish a deaf and dumb infant from a mentally defective one. The intelligence of his gestures and expression, his obvious interest in surroundings, his cleanly habits, and the ready use of his hands, will, however, usually help us to recognize that nothing worse than deafness is present.

RECURRENT CONVULSIONS.—The periodic recurrence of convulsions without obvious cause, when it continues over a long period of time, generally indicates the presence of mental impairment. This may be simply the effect of the fits, but more commonly the mental defect is just another symptom of the brain lesion which is causing them.

Terminology.—Mental deficiency and amentia have come to be used as synonymous terms. They cover the field of mental defect in childhood and imply a failure in the development of the mind. The causes productive of amentia may be germinal in origin, or arise previous to, at, or soon after birth. The term "dementia" comes into use when the mental

defect has its onset after a time sufficient for mental development to have taken place. Dementia præcox is a good example of the latter type, and one which may be met in children, usually about puberty, sometimes earlier (see Heller's dementia p. 1139). Amentia is subdivided into three grades, which have received legal sanction, and the sense of the terms as recognized by law should be retained as far as possible in their general usage to avoid confusion. At the lowest end of the scale there is the "idiot," next the "imbecile," then the "feeble minded." A fourth term, the "moral defective," is also in use, but this term, as legally defined, can scarcely be applied to children.

Above these, in that ill-defined space between the abnormal and the normal, there are two gradations, the "dull" and the "backward." In addition, it must be remembered that mental deficiency is not infrequently suspected in children in whom environmental conditions, and not any intrinsic impotence of the mind, are in reality responsible for the abnormal state. Such cases require careful differentiation, as, under suitable conditions, a healthy state of mind can be regained.

Definition of terms.—The Mental Deficiency Act of 1927 defines mental defectiveness as "a condition of arrested or incomplete development of mind existing before the age of eighteen years, whether arising from inherent causes or induced by disease or injury." The liberal age-span, up to the eighteenth year, gives scope for the recognition of milder degrees of defectiveness difficult to assess in the earlier years of life, and for the inclusion of children mentally afflicted by the sequelæ of such conditions as epidemic encephalitis. It also defines certain classes of mentally defective persons who may under certain conditions be dealt with under its provisions:

(*a*) *Idiots*, "persons in whose case there exists mental defectiveness of such a degree that they are unable to guard themselves against common physical dangers."

(*b*) *Imbeciles*, "persons in whose case there exists mental defectiveness which, though not amounting to idiocy, is yet so pronounced that they are incapable of managing themselves or their affairs, or, in the case of children, of being taught to do so."

The imbecile is incapable of laying out his earnings. He may be employable in some simple and routine task, but he will fail if anything be left to his own initiative.

(*c*) *Feeble-minded persons* are those in "whose cases there exists mental defectiveness which, though not amounting to imbecility, is yet so pronounced that they require care, supervision and control for their own protection or for the protection of others, or, in the case of children, that they appear to be permanently incapable by reason of such defectiveness of receiving proper benefit from the instruction in ordinary schools."

(*d*) *Moral defectives*, "persons in whose case there exists mental defectiveness coupled with strongly vicious or criminal propensities and who require care, supervision and control for the protection of others."

This last definition is a difficult one. Morality, depending on a series of associations and judgments acquired by the individual from his

experiences in life, can hardly be said to exist in the earlier years. The young child is amoral, and a full appreciation of moral issues does not come prior to puberty. This group must include both cases of normal intelligence combined with a psychopathic personality, and cases of defective intelligence with a secondary undevelopment of moral sense, which could more appropriately be certified as feeble-minded.

So far as education is concerned, a distinction has to be made between mentally defective children and those that are merely dull or backward. These latter terms are not legally defined, but it is usually accepted that a " dull " child is one suffering from an innate condition, and that, however much attention he receives, he will never be able to make progress at the normal rate, or to the same extent as his fellows. The " backward " child is retarded by want of education from such a cause as ill-health, but can in time make up on, and successfully compete with, his fellows.

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Causation and classification

The difficulty of making a really satisfactory and scientific arrangement of the numerous varieties of disease, of which mental defect is a prominent feature, seems to be insuperable, and it is as easy to criticize effectively all the classifications that have as yet been put forward as it is difficult to frame a better.

Some sort of classification is necessary, and the most practically useful for clinical purposes is that of Tredgold. He divides all cases of mental defect into two groups, according as they are *primary*—the cause of which is intrinsic, endogenous or germinal—or *secondary*, due to extrinsic or exogenous factors. Among older children and adults, the first of these groups includes, according to Tredgold's estimate, about 80 per cent. of all the cases, and the second about 20 per cent.

The following further subdivision of these two groups, which is a modification of Tredgold's classification, is offered tentatively to give some idea of the number and variety of the clinical types of disease which are characterized by mental defect.

(A) Primary amentia. Due to—

" Simple primary " arrest of development of cerebral neurons. (This group probably includes many types not yet differentiated. Many of the cases are characterized by epileptiform convulsions.)

True microcephalus.

Mongolism.

Tuberous sclerosis ; epiloia.

(B) Secondary amentia, as a result of—

In intra-uterine life.	1. Congenital hydrocephalus. 2. Congenital porencephaly. 3. Microcephaly (other than the type mentioned above). 4. Cerebral diplegia (some degree of amentia is commonly present). 5. Rh factor incompatibility ?

At birth.	1. Cerebral diplegia 2. Hemiplegia.	some cases due to the effects of anoxæmia.
In extra-uterine life.	1. Trauma and vascular lesions. 2. Encephalitis. 3. Meningitis. 4. Hydrocephalus. 5. Congenital syphilis. 6. Epilepsy. 7. Endocrine deficiency ; cretinism.	

PRIMARY AMENTIA

Simple primary amentia.—In its causation, most writers are agreed that *heredity* is the most important influence at work. The genetic defect may reveal itself in a single or in several members of a family ; Martin has described " a pedigree of mental defect showing sex-linkage." In Still's lectures on " Place in family as a factor in disease," he noted the highest rate both for mental deficiency (excluding mongols) and for congenital abnormalities in the first-born.

Phenylpyruvic oligophrenia, or Fölling's disease, is a type of primary amentia, with a high percentage of familial cases, 67·8 per cent. Its incidence is estimated at about 1 in 25,000 of the general population. The condition is distinguished by the presence of phenylpyruvic acid in the urine, a finding which does not occur in the mentally normal relatives. A few drops of a 5 per cent. solution of ferric chloride added to the acidified urine produces a dark green colour, which slowly disappears. Jervis describes these defectives as often having a normal stature, attractive features, usually blond with blue eyes, an increased muscle tone, and an I.Q. of 20 to 50.

Symptoms.—This class includes all degrees of mental impairment from the slightest to the most profound, and the symptoms vary considerably according to the amount of intelligence present. The I.Q. related to the different degrees of defectiveness is, under 25 per cent., idiocy ; 25 to 50, imbecility ; 50 to 75, mentally backward and needing special education. In the worst cases, the condition is that of utter idiocy. The baby is obviously abnormal from the first—dull and apathetic, paying no regard to his surroundings. He often does not know his mother by sight, though he may turn at her voice ; sometimes he only recognizes her, if at all, by the way she holds him. A considerable majority suffer also from frequently recurring convulsions, which commonly take the form of *petit mal*. As such, the fits are apt to escape notice, or to be put down to indigestion by the parents.

In less severe cases, the symptoms may be much less noticeable, especially during infancy. Dentition and the closure of the fontanelle proceed as in normal children, and, as there is no paralysis or gross deformity and no markedly abnormal gestures, the child's want is often overlooked during the early years of life. Someone, however, generally notices that the baby is strangely long in showing an interest in bright lights and moving objects, and is late in recognizing his parents and the

other children. He is also backward in learning to use his hands, and in holding up his head, in sitting up, in standing, and in walking. When he does learn to walk, his gait for long remains clumsy and like that of a younger child. Such children often go with their heads slightly forward and their arms hanging in front; their feet are planted far apart, their pelvis moves too much in walking and the joints of their lower limbs too little. Their hands, too, remain clumsy and nerveless. A common symptom is a more or less constant dribbling of saliva. Proper control of the bladder and bowel is often long in being acquired—sometimes not until four, six, or even eight years old—and yet it may become quite normal in time. Convulsive attacks are common, though not so frequent as in the severer cases.

The mental symptoms may not be prominent at first, but the children are generally late in starting to speak, their speech is indistinct and the words badly pronounced. When they reach an age at which they should be beginning to learn some sort of lessons, they are found to be hard to teach, because they are unable to give their attention continuously for any time to the same thing. Even when they are doing what they like, they seem incapable of perseverance. Many are deficient in affection, and all in common sense. They lack self-control, laugh and cry without sufficient reason and often get into causeless passions. A common indication of their defect is their inability to learn their way about the house, or streets in the neighbourhood of their homes.

Mild cases of mental defect, such as form the proper pupils of the "special schools," generally pass unrecognized through infancy and early childhood. They have wits enough to perform passably the actions of babyhood. It is only when the time comes that they should leave hold of their mother's apron-strings that they show their utter unfitness to guide themselves properly and to keep pace with their fellows. The facts that they are late in walking and talking, and that they are long in losing their baby speech and babyish ways of behaving, are thought little of. When their schooltime comes, however, their teachers soon discover their weakness. The mental and manual work they do are very much below the average. They are often amiable, but facile and unsatisfactory, with no strength of purpose, little practical sense of right and wrong, and no proper realization of their responsibilities.

In later life, their weakness of will and lack of self-control and of common sense are constantly landing them in trouble whenever they leave the shelter of home and come in contact with life outside. If they can be kept carefully guarded in wisely managed homes, they remain for life good and happy children.

Pathology.—There is no constant appearance of the brain in primary amentia, no essential differences in convulutional complexity, depth of cortical grey matter, nor in the number of nerve cells in the cortex in the ament compared with the normal. Stewart remarks that the brains of low-grade defectives show wide variations in their structure, and stresses the importance of quality of cells, the richness of their interconnections and vascular supply for normal functioning.

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MICROCEPHALIA VERA

Microcephalus.—The term *microcephaly* was used by many as synonymous with "small-headed," and any child with a cranial circumference of less than 17 inches was called "microcephalic," although his mental endowment might be normal. It is better to reserve the term for the small and fairly well defined group of cases of "true microcephaly." These are distinguished by very small heads, which are also of a peculiar form, having a narrow forehead, recession of the fronto-parietal bones, a pointed vertex and flattening of the occiput. Other characteristics are a receding chin, large outstanding ears, and, as the features become more fully developed, a prominent nose (fig. 336). Closure of the fontanelle takes place either before birth or soon afterwards.

Fig. 336.—Microcephalic Idiot, Circumference of Head 13¾ inches.

Many adverse factors capable of affecting the germ cells or the young embryo may produce microcephalia vera. In *familial* microcephaly a recessive type of heredity is believed to be the cause. Whitney recorded four instances of microcephalic twins, three identical and one dissimilar, and up to seven cases of microcephaly in one family. Halperin puts possible parental consanguinity at about 10 per cent. Exogenous causation of microcephaly can follow radium exposure of the fœtus *in utero*. Murphy found that of seventy-four fœtuses heavily irradiated before birth twenty-five were congenitally deformed, and of these seventeen were microcephalic idiots. Von Monakow stated that the pathological factors acted in the embryonic period, resulting in "the crystallization of a phase (of development) which in normal evolution would have been only transient." Greenfield and Wolfsohn claim that these factors are at work before the fourth month of fœtal life, and describe both agyric and complex microgyric forms of brain in microcephalia vera (fig. 337).

Symptoms.—The child's appearance is characteristic if the case is a

well-marked one, but in early infancy the disproportion in the relative sizes of the head and body are not always striking. Later, as the body grows at a fairly normal rate, the smallness of the head becomes more conspicuous. By the sixth month of life, when the normal child's head should have grown from a birth measurement of 13 or 13½ inches to one of 16 inches or thereby, in the microcephalic it is still only 13 or 14. At twelve months it may be 14 to 14½ inches instead of 18; at two years, 15 to 16 instead of about 19. In older children, the circumference may remain only 15 inches, although sometimes it reaches 18 or even 19 inches. The early closing of the fontanelle is an important point in the diagnosis. In some cases the palate is highly arched.

The first teeth appear at the usual time, but the child generally does

Fig. 337.—Microcephalic Brain, showing Simple Type of Convolutions. (Scale in inches)

not walk until the third or fourth year, or even later. As age advances, there is a tendency to hold the head stretched forward, and this, along with the rapid way it is jerked from side to side, gives rise to a curious "bird-like" aspect, which has often been remarked upon. Speech is scanty and slowly acquired; control over micturition and defæcation is sometimes late in coming, and in bad cases may never be quite satisfactory. There is often a history of convulsions. In true microcephalus there is generally no real paralysis, but during the early months of life many of these children show a striking degree of spasticity. This apparently represents an exaggeration of the normal hypertonicity of healthy new-born children, and probably depends on the backward development of the cortex. It passes off completely as the children grow older.

True microcephalics are always mentally defective, but not all equally. They vary between complete idiocy and states of feeble-mindedness. They are generally restless, inquisitive and greedy, quite devoid of affec-

tion, and dangerous to smaller children and to animals. When the head is not too undersized, however, there may be a small degree of intelligence combined with a more kindly disposition, and the child may be capable of a slight amount of education.

Prognosis.—The outlook, both as to length of life and as to mental improvement, is generally bad. The children are usually more or less delicate, and many of them die in early childhood. In rare instances they live to old age.

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MONGOLISM

In 1866, Langdon Down first drew attention to a group of imbecile children whose features had a curious resemblance to those of the lower Mongolian races. This mongoloid type was further investigated by Arthur Mitchell and John Fraser and many others, and was soon recognized to form a class by itself, with physical attributes of so definite a

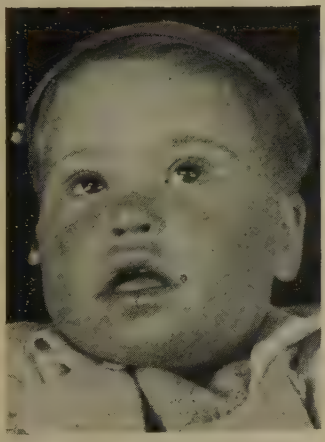

Fig. 338.—Mongolism: Boy aged One Year Four Months.

Fig. 339.—Mongolism: Boy aged Four, showing Facies, Epicanthic Folds, and Protruded Tongue.

character that all cases presented a striking "family likeness" to each other.

Symptoms.—Mongolism affects the conformation of the entire body, but its signs are most readily seen in the face, head and hands. The cranium is invariably small, rounded, button-like, devoid of eminences, and the occiput is commonly flattened. The eyes are frequently too near

to one another, but their chief characteristic is the obliquity of the palpebral fissures, the outer angle pointing somewhat upwards. In many, the epicanthic fold of skin at the inner canthus is strongly developed. This peculiarity tends to be less noticeable in later childhood than in infancy. Squint is common (9·4 per cent.); nystagmus even more so (12·3 per cent.); and partial ptosis is sometimes observed. It has been pointed out by Pearce, Rankine and Ormond that a peculiar spotted form of lamellar cataract is often present in mongols over nine years old.

The nose is usually snubbed, and the nostrils in early life have often

FIG. 340.—MONGOLISM: GIRL AGED NINE YEARS, SHOWING EPICANTHIC FOLDS, FISSURED TONGUE, AND CHARACTERISTIC HANDS.

a peculiar triangular shape. Adenoids are frequently present and may produce severe symptoms owing to the small size of the naso-pharynx. The palate is usually high and narrow. A more characteristic feature is the protrusion and sucking of the tongue, which is specially common in the early years. The tongue may be large and long, but its protrusion is rather to be accounted for by the shortness of the mouth. About the sixth or ninth month, the papillæ enlarge in increasing numbers, and the surface of the tongue assumes a raw granular appearance. Later, during the third or fourth year, deep transverse fissures form across the dorsum, and it is rare to see a mongol over six years in whom this fissuring is not present, though the *scrotal* or *striated* tongue may also be seen in other types of defectives.

The ears generally show some deformity. They are often small, rounded and simply convoluted, and stand out from the head more than usual. The teeth are usually late in erupting and are apt to become yellow and decay early. The mucous membrane of the lips is often dry and fissured. The hair, usually of a light colour, is apt to be dry and poor in the older children, and the skin is often harsh and rough. Thickening of the eyelids, due to blepharitis, is frequently observed. In babies, both the skin and the hair are soft and natural.

The limbs are small-boned and soft, and rather shorter than normal compared with the trunk. Their ligaments are so lax that the joints can usually be easily hyperextended. When sitting, the mongol tends to cross the legs, with the soles of the feet turned upwards and outwards. The hands are usually coarse and clumsy, with fingers which are thick for the size of the hand, but not so square-tipped as those of cretins.

FIG. 341.—MONGOLISM: GIRL AGED FOURTEEN MONTHS, SHOWING GENERAL APPEARANCE AND HYPEREXTENSIBILITY OF JOINTS.

FIG. 342.—MONGOLISM: HANDS OF BOY AGED FOUR YEARS.

The thumb is short, and the little finger, in more than half the cases, is both dwarfed and somewhat curved towards the ring-finger. On the palms, there is a confusion of lines, like those on a piece of crumpled paper which has been unfolded. In the feet, Brushfield has drawn attention to the frequency of a wide gap between the first and second toes, with a deep line running backwards from this space to the sole.

Voluntary muscular movements are slow of being acquired. Often the baby does not hold up his head until the sixth or even the ninth month, or sit until the end of the first year, or later. The average age of learning to walk is about three and a quarter years, and the gait is often very clumsy. The grasp also is usually feeble and fumbling. Speech is delayed in most cases, is guttural and indistinct, and often scanty. In the worst cases, the child can scarcely say anything. In disposition the mongol is bright, lively, imitative and affectionate, and shares a fondness for rhythmic musical noises with other mental defectives. Mentally,

most mongols are idiots or imbeciles, but some can in time be taught to read. Their mental age, however, as opposed to their real or chronological age, rarely exceeds seven.

In addition to the numerous small defects of conformation above described, we often meet with other congenital abnormalities of various parts.

The following is a list of those found in the examination of 138 cases :

Cleft palate	1	Hypospadias	1
Congenital cataract	1	Undescended testicle	5
Supernumerary tragus	2	Post-anal dimple	1
Congenital heart disease	22	Congenital diastasis of recti abdominis	1
Club-foot	4	Umbilical hernia	2
Genu recurvatum and no patella	1	Inguinal hernia	1
Cubitus varus	4	Congenital stenosis of rectum	1
Syndactyly of toes	1	Congenital stenosis of large intestine	1
Dwarfed terminal phalanges of fingers with deformed toes	4		

Prognosis.—Mongols are apt to take infective diseases, and to have them badly. Catarrhal affections of the eyelids, nose, throat and intestine are common. Bronchitis is especially frequent, and tends to end in collapse and broncho-pneumonia. Mongols surviving infancy are often fairly robust. Those who live beyond forty, however, soon get to look old and frail. Glutamic acid, 12 gm. or more daily, in three divided doses, is stated in a preliminary report by Zimmerman, Burgemeister and Putnam (1949) to have effected a rise of 1 to 20 points in the intelligence quotients of seven typical mongols.

Frequency.—Mongolism is not uncommon in this country. The crude absolute incidence is in the region of 1 in 10,000 births (Penrose). The percentage among mental defectives varies with the source of the estimates, whether coming from institutions, or from children's hospitals. On the one hand, Shuttleworth states the proportion as 5 per cent. " of adult aments." On the other hand, Still found no fewer than 22 per cent. out of 350 imbecile children, and John Thomson considered 20 to 25 per cent. a fair estimate. The disparity between the two groups of figures is explained in the following ways : (1) a considerable number of mongols die during the first few years of life ; (2) many cases seen at children's hospitals remain at home and do not enter institutions. It is, therefore, easy to understand how statistics drawn from children's hospitals give a far larger proportion of mongols than those taken from institutions to which only older children are admitted.

Ætiology.—The brains of some mongols are of an embryonic convolutional type, suggestive of some inhibitory influence upon the development of the embryo some time before the end of the eighth week of pregnancy.

Shuttleworth has spoken of mongols as " exhaustion products," as over one-half are last born. They are often the last children of elderly

parents, or of mothers who are near the end of their child-bearing period. In an analysis of 294 cases, the average age of the mother at the birth of the mongol was thirty-seven and a half years, and in only thirty-eight cases was the mother under thirty years. In a considerable number of cases the mother was older than the father. The significance of these facts must not be over-rated, as a mongol may be the first-born of young parents, or occur in the middle of a family and be followed by healthy children.

There are so far fourteen recorded instances of identical twins both mongols (monozygotic), and fifty-eight pairs of dizygotic twins of the same or opposite sexes and one member a mongol. Jervis, furthermore, records four instances of dizygotic twins, both mongols, but each pair was of a similar sex. Penrose considered that mongolism depends upon a chromosomal factor recessively or dominantly inherited, but it is possible that external agencies play a part.

Pathology.—In an examination of ten brains from mongols from seven months to forty-two years of age, Davidoff gives the following particulars; weight below average for age; disproportionally small size of cerebellum and brain-stem; general appearance varying from superficially normal to convolutional embryonic simplicity with an absence of secondary gyri; and microscopically the quantity of cortical ganglion cells appeared to be low.

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CONGENITAL HYDROCEPHALUS AND PORENCEPHALUS

These conditions are described on page 1208 and page 1290.

EPILOIA: BOURNEVILLE'S DISEASE: TUBEROUS SCLEROSIS

Tuberous sclerosis, or hypertrophic nodular sclerosis of the brain, is a rare heredo-familial affection. Mental deficiency is a constant symptom and is associated in some cases with epilepsy and adenoma sebaceum. This triad is easily recognizable clinically and is known as *epiloia*. In addition, congenital tumours may be present, teratoma, rhabdomyoma in the heart, adenosarcoma in the kidney, and tumours of the spleen

and lungs. Retinal tumours, or neurological masses (phakomata), sometimes with associated vascular nervoid lesions, were observed in six, bilaterally in three, out of twenty cases by Hall.

Fig. 343.—Epiloia.
(From a photograph supplied by Dr. Brushfield.)

Ætiology.—The developmental defect of the cerebral hemispheres dates from early fœtal life. It is an embryonic tissue dysplasia, other examples of which are diffuse neurofibromatosis (von Recklinghausen's disease), and melorheostosis (a bony hyperostosis of axial distribution producing swelling of a part or of the whole of a limb and confined usually to only one limb, and noticeable even from birth). Hall has described a case of epiloia in association with von Recklinghausen's disease, and another in association with melorheostosis, which combinations are probably not accidental. He thinks the latter combination can be explained on the basis of a mesodermal defect of unusual distribution and type. Penrose considers *epiloia* to depend on a single dominant gene.

A strong psychopathic taint is often present in the family histories of epiloiacs, and among the relatives there may be instances of adenoma sebaceum alone, and of adenoma sebaceum and epilepsy without mental defect (Critchley and Earl).

Symptoms.—Mental deficiency is usually obvious from birth. Convulsions, grand or *petit mal*, occur in most cases, beginning during the first weeks or months of life, or delayed until late childhood. The adenoma sebaceum, characteristically in a butterfly distribution on both sides of the face and across the nose, appears at about the fourth or fifth year.

Sometimes the intellect is apparently normal for a varying period of years, and shows obvious signs of deterioration after the convulsions have persisted for some time. The mental state becomes one of idiocy or of imbecility. Physically, the patients are often ill-developed and present stigmata of degeneration, but spastic paralysis rarely makes an appearance. Most of the patients die either during childhood or in early adult life.

Pathology.—The brain on section shows whitish nodules of sclerotic tissue varying in size from a pea to a walnut, most numerous in the grey matter of the cortex, palpable also in the white matter, but rarely present in the cerebellum. The masses are most numerous in the frontal and temporal lobes. Microscopically, they are seen to consist of glial fibres and large cells, possibly spongioblasts.

Between the nodules small areas of cavitation occur. Tumour-like accumulations of ependymal cells—candle gutterings—may be seen in

relation to the ventricles. In a few cases a large gliomatous growth has also been found in the cerebrum.

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SECONDARY AMENTIA

Rh incompatibility may yet be proved to be a factor in the developmental pathology of mental deficiency, as well as giving rise to kernicterus in some cases of erythroblastosis fœtalis. From a survey of investigations on this problem, in children with specific types of feeble mindedness, such as mongols, spastic diplegias, birth trauma, the Rh-positive and -negative distributions in the mothers was about the normal average. But of fifty-six cases of undifferentiated mental deficiency a suggestive increase in the Rh-negative factor in the mother was found, fourteen out of fifty-six, of which eleven had Rh-positive children. In this group the Rh-negative ratio of the mothers is more than twice the average for the general population (Cook).

Amentia due to gross cerebral lesions.—Any form of gross cerebral disease or injury which causes paralysis is apt to be accompanied by more or less impairment of the mental functions. Cases of this kind in which no intellectual weakness can be made out do, indeed, occur, but are quite exceptional. Even when the parents regard the child as normal in mind, at least a degree of mental instability, a tendency to epileptic fits, some emotional weakness, or some other slight mental peculiarity which shows that the psychic centres have not altogether escaped damage is usually found. In many cases the mental symptoms are more marked than the paralysis. The cranial circumference in cases of cerebral disease originating *in utero* is frequently found to be subnormal. Porencephaly is sometimes discovered in the brains of aments. In true porencephaly there is a developmental defect, whereby a communication exists between the surface of the brain and the lateral ventricle. Its commonest situation is in the inferior or in the middle parts of the brain, and the deformity may be bilateral. Pseudo-porencephaly is the result of hæmorrhagic or inflammatory lesions, which give rise to local atrophy and the formation of a cavity. The cavity is irregular in shape, interrupting one or more convolutions and is filled by encysted cerebro-spinal fluid.

Far the commonest type of paralysis associated with amentia is spastic diplegia. This arises either from intra-uterine lesions, or is due to asphyxial anoxæmia and its consequences at birth. Many of these children have great determination and not a little common sense, so that they sometimes improve surprisingly under careful training. In cases of hemiplegia from birth injury, the mental symptoms are usually less severe than in those of diplegia.

The amentia associated with chronic hydrocephalus of congenital

origin is generally of rather a mild type, and the children are docile and well-disposed, although lacking in energy and initiative. In the form of chronic hydrocephalus which follows basic meningitis, the mental defect is generally more severe than in the congenital cases. Cases of cerebral damage from cerebro-spinal meningitis, apart from hydrocephalus, and cases of encephalitis in early life, are usually characterized by serious mental enfeeblement, and the prognosis as to improvement is not good.

Infantile cerebral degeneration, amaurotic family idiocy, is discussed elsewhere (p. 1329).

Epilepsy in relation to mental defect.—As has already been seen, epileptic seizures are among the commonest clinical phenomena met with in simple primary amentia and many other types of mental defect. They occur, indeed, in all its varieties, but with great rarity in cretinism and mongolism. In the great majority of instances, when fits occur in mentally deficient children, they are secondary to the main organic disease which is causing the amentia, and are not its cause. At the same time, their repeated recurrence has generally an obviously bad effect on the mental state; the child ceases to improve while they go on recurring, and brightens up when they pass off, or there may be progressive mental deterioration.

Moral deficiency.—The ordinary mentally defective child is often notably deficient in moral appreciation, although it is the intellectual want that is the main characteristic. Occasionally, however, children are met with who, in spite of an almost average capacity for lessons and for looking after themselves, seem to have been born without the power of appreciating the rights of others. An ordinarily careful upbringing fails to give such children any due sense of the difference between right and wrong, and no amount of punishment or of persuasion is able to break their habits of telling lies, stealing, and doing cruel and indecent actions. Marked instances of this kind are, fortunately, rare, but they are occasionally met with, even in children as young as five or six years old.

For their own sakes, as well as for that of the community, morally deficient children should, as soon as possible, be sent to some school or institution where they will be constantly under the supervision of teachers or practitioners with special experience in the training and investigation of young children. Once their confidence has been gained, the child may by his words and actions reveal associations which have had an inhibiting effect on the normal course of mental growth and have fixed his emotional reactions at a stage far below his intellectual level. It will usually be found that the child has been moulded in his emotional reactions both by the general nature of the home environment and even more by his special personal relations with his parents and nurse. He may have suffered from inattention, but far more often from over-attention and spoiling. The child quickly learns how to behave so as to secure his desired ends in the home, and is slow to change his attitude when placed in a less sympathetic environment, while if his plunging into the world is long delayed he may even have almost entirely lost the capacity for

adjustment. The treatment needed in such cases approximates more to that for the early phases of the psychoneuroses than to that for those who are intellectually defective, and cannot satisfactorily be carried out in the home.

GENERAL TREATMENT

The treatment of the mentally defective child is mainly a question of wise training. It must be borne in mind that though the condition is essentially incurable, a large number of defective children are capable of some kind of improvement under judicious management. It is extremely desirable to focus the attention of parents on such aspects of their child's deficiency as are most likely to be improved by individual attention from them. This is not only best for the child itself, but it also brings the parents in the most natural way to see what are the child's limitations. Such knowledge will prevent them from forming false hopes such as often lead to unnecessary pain at a later date, and prepares them to face sensibly the hard problem of the child's future. Most parents find it exceedingly difficult to believe that any child of theirs can really be wanting in intellect, so that if the fact is urged upon them before their own observation has prepared the way they are apt to reject it with more or less annoyance, while they lend a ready ear to foolish people who tell them that, at seven, or at fourteen, or at some other age, there is sure to be a complete and spontaneous recovery.

The chief aim of treatment must be to make the defective child more capable of performing the common actions of everyday life like other people, and so to form his manners and conduct that they may be unobjectionable to those with whom he associates. It is also important to cultivate a sense of responsibility, and to induce him to exert his own powers of body and mind, and above all, his affections. It is a true saying that occupation is the key to success in dealing with mentally defective children, whilst idleness is to them the root of all evil.

In the course of mental training the child must be encouraged in the voluntary use of all his muscles; this improves his strength and his co-ordination and is helpful in checking the purposeless automatic movements which are sometimes present. For younger children and those who are severely affected, simple actions, such as clapping the hands, playing with a rattle or with a suspended ball, may be all that is possible. For others ball games, walking between the rungs of a ladder placed on the ground, trundling hoops and the like are helpful, while a sense of rhythm may be developed by singing, games, dancing or skipping. Threading beads, building with bricks, or coloured blocks to make pictures, all sorts of kindergarten games, and indeed almost any play with toys, are useful.

The child should be encouraged to notice things and to compare their characters—roughness and smoothness, hardness or softness, heaviness or lightness—colours, shapes, taste and smell. For this purpose almost any kindergarten or Montessori material can be utilized effectively. The mentally defective child should be encouraged to help in the house

and to imitate the actions of others, in play if need be, though he may need to be taught many things which normal children do of their own accord without any teaching. At first easy successes should be planned for him; if he deliberately wants a thing, tries to get it and succeeds, this is a most valuable and pleasant lesson, but he must not be disheartened by being given tasks beyond his capacity. In the case of a baby, if he likes a noise, let him have something he can make it with for himself. Never let the mother or nurse go on doing for the child anything that he can himself be made to do for his own pleasure.

Cultivation of character is all-important and includes many things. One of the first of these is the training of the child in keeping himself clean and in letting his mother know when he requires to be attended to. Some mentally defective children can never be taught cleanly habits, but in most cases, even where there has been complete incontinence in early childhood, the child may in time, by persevering attention, be trained to have completely normal control. General cleanliness and tidiness in person and dress are also constantly to be insisted upon, and the child encouraged to take a pride in having everything about him nice.

All sorts of "bad habits," to which these children are particularly prone, must be watched for and checked at their earliest beginnings, preferably by deflecting the child's attention to something else rather than by reproval which may only attract his attention to the action and induce him to repeat it for the sake of keeping under notice. This refers not only to such habits as thumb-sucking, dirt-eating and masturbation, but to unpleasant tricks of manner and expression, grimacing, making unpleasant noises, unrestrained gestures and the like. These do the child much harm by drawing attention to the deficiency and make him objectionable to others.

The acquisition of good manners, good temper and decency of conduct, an ability to speak clearly, and the use of the knife and fork is usually of more importance than that of reading and writing. Thoroughness in everything, so far as it is practicable, should be the watchword; the mother must never acquiesce in the child doing less than his best because he is weakly. A habit of prompt obedience is of course of the greatest value. The child should not be too far protected from the physical consequences of minor indiscretions, for the lesson of nature is the one which is more clearly understood and borne in mind even by the defective child. Even in comparatively low-grade cases we find ideas of fairness, honesty, truthfulness, unselfishness and affection which should be watched for and encouraged to the utmost.

Somewhere about the age of six or seven the question of school has to be considered. Wherever possible this is an undoubted advantage as much to a defective as to a normal child, for unless he can associate with other children of about his own age and mental level he misses the great boon and stimulus of society and healthy rivalry. Where the home conditions are suitable and a school conducted by those who have real experience in the handling of mentally defective children is available, this may suffice. For those children who would normally attend a

public elementary school adequate provision in the form of special schools has been made by the education authorities of most of the larger towns in Great Britain. At these schools the curriculum is specially adapted, and much time is devoted to manual activities leading up to definite trade training.

With special education in these schools or in institutions, a large proportion of the feeble-minded can be trained to be self-supporting in some humble occupation, and a smaller proportion, which have been certified as feeble-minded in early childhood, can be decertified at or before the age of sixteen years. At the normal age in adolescence of acquiring independence and of becoming a wage-earner, the problem of socializing the feeble-minded presents many difficulties. Special training makes it possible for many of these cases to become self-supporting, but the environment requires careful consideration. Being of weak intellect they are easily led astray, and on falling into bad company readily enter the ranks of the juvenile delinquents. Therefore, some form of supervision continues to be essential for their welfare.

INSTITUTIONAL TREATMENT

The question whether the mentally deficient child should be kept at home or sent to an institution is at times difficult to answer. During the first six or seven years of life there can be no doubt that the advantage of a good mother's constant care outweighs all benefits an institution may offer, and in some cases the same may be said with regard to older children. Generally, however, if they are at all trainable, there are strong reasons in favour of institutional treatment as age advances. If the child has been carefully brought up, he will probably do no harm to his normal brothers and sisters; but this is by no means always the case. Where younger children are imitating a defective the parents should be urged to consider their interests first and foremost. For himself, the routine of a well-conducted institution is generally far happier than life at home. For one thing it is extremely discouraging for him, as he grows older, to be associated in his work and play with normal children; not only are they apt to tease him, but the fact that by no effort can he do anything nearly as well as they do is very demoralizing. For another, the home surroundings of most mentally defective children are such that they cannot be allowed much freedom while living with their parents, and therefore even their limited capacities do not get so full a scope as is possible with the wide range of facilities for occupation and instruction available in an institution.

Should the parents decide to place a mentally defective child in an institution, two medical certificates will be required—one to be given, as a rule, by the ordinary medical practitioner and the other by a practitioner recognized for the purpose by the Board of Control or by the Local Authority under the Mental Deficiency Act. These certificates are in a specified form in which the class of defect and the grounds upon which the diagnosis rests must be stated, distinguishing between the facts

observed by the certifying practitioner and those of which he has been informed by others. The examination must have taken place within seven days of the date of the certificate. The necessary forms and a statement of the particulars of the case to be filled by the parent are usually obtained from the authorities of the institution. These details have been modified for the child between two and seven by the Education Act 1945.

Should a defective child be in need of care and training which cannot be provided on account of lack of means, the parent should apply in the case of a child over two years to the local education authority for advice and help. The teaching of the defective child has its own methods and requires skill and devotion, and is well described in Margaret Macdowall's textbook "Simple Beginnings in the Training of Mentally Defective Children" (London, 1930).

CHAPTER XXVII

ORGANIC DISEASES OF THE NERVOUS SYSTEM

W. G. WYLLIE, W. McKISSOCK AND I. A. B. CATHIE

Clinical examination of the infant and child.—Only a limited co-operation can be expected from the young child, still less from the infant, so that a full and detailed history must be obtained from the parents. This essential inquiry must include not only the past and present health of the child, but also the family history. To ascertain facts of diagnostic value, the interrogation must be conducted patiently, and in such a way that answers are not suggested to the witness by leading questions. An examiner, hasty or relying overmuch on his intuitive faculty, is often led astray into asking questions congenial to his preconceived opinion of the case, and will receive affirmative responses. From the same parent, interviewed more cautiously by another, a history with a different significance may be obtained.

In paralysis of obscure origin, the past history including the manner of the child's birth is of the greatest importance. In the present history the order in which the various symptoms appeared must be clearly determined. It is the early symptoms in a case of cerebral tumour which lead to a correct localization, and not the later ones resulting from increased intracranial tension, although these often become the more conspicuous. Frequently in cases of nervous disease parents will attribute the paralysis to the effects of a fall. Although this opinion is commonly erroneous, yet the nature and severity of the fall and its immediate effects must be calculated, as the results of such trauma can be incommensurate with its apparent severity.

First, notice is taken of the child's general expression, behaviour, intelligence and attitude. Any abnormality in the size and shape of the head will be observed. The method of further examination will naturally be controlled by the site and nature of the paralysis, but no case has been fully investigated until inspection has included the cranial nerves, the motor and sensory systems and the state of the reflexes.

THE CRANIAL NERVES.—The first nerve, that of smell, is rarely capable of being examined in the young child. The second nerve, that of sight, is tested in the infant by noting if the eyes will follow moving objects, and in the older child with Snellen's test type. Defects of the visual field, hemianopia from lesions of the visual pathways at or behind the optic chiasma, can only be estimated in the young child by observing its response in moving its eyes towards bright objects moved into the fields of vision from the sides. Changes of the optic fundi revealed by ophthalmoscopic inspection include optic atrophy, papillœdema, tubercle of the choroid, choroiditis, retinitis and hæmorrhages.

The third, fourth and sixth nerves are examined together by testing the movements of the eyes, noting any weakness of the levator palpe-

brarum, the reaction of the pupil to light and on accommodation. Inequality of the pupils is looked for. Such inequality, apart from paralysis of the third nerve and local conditions of the eye, may be due to affection of the fibres of the cervico-sympathetic on one side. An Argyll-Robertson pupil is not a common condition in a child, but when it occurs it is, as in the adult, suggestive of syphilis. It may also be produced by lesions of the corpora quadrigemina.

In *ophthalmoplegia interna*, the pupils usually of both eyes are inactive both to light and on convergence. The fibres of the ciliary ganglia, or the ganglia themselves, are affected. This form of ocular palsy is most often seen in post-diphtheritic neuritis.

In *ophthalmoplegia externa*, numerous ocular muscles of one or both eyes are paralysed, due to lesions affecting the nuclei of the oculomotor nerves or their trunks within the brain-stem, as occurs in epidemic encephalitis, or to lesions of the extramedullary portions of the nerves, as in cavernous sinus thrombosis. Paralysis of conjugate movements, commonly in a lateral direction, is most often due to a nuclear lesion of the sixth nerve which also involves its fibres of communication in the dorsal longitudinal fasciculus with the nucleus of the third nerve on the opposite side. In such a case there is no weakness of the internal rectus on convergence of the eye opposite to the one in which the sixth is paralysed. Defective upward movement of the eyes is rarely seen except in lesions of the superior corpora quadragemina, and may be due to the pressure effects of a tumour in that neighbourhood. *Supranuclear ocular paralysis* is indicated by an inability of the patient to move the eyes voluntarily in some direction, yet reflex movements may still be possible as in following a moving object. In their extra-medullary portions, the sixth nerve is the one most commonly damaged, owing to the length of its course within the skull. External rectus palsy is often produced by meningitis and raised intracranial pressure due to cerebral neoplasm. In the first few years of life, diplopia in a paralytic squint is rarely complained of, as binocular vision or the power of fusing two images is not fully developed ; so that the reception of two images at this early period does not give rise to the confusion that it produces in the older child or adult.

Of the other cranial nerves, the seventh is the most commonly affected. When the lesion is in the nucleus or the peripheral portion of the nerve, there is weakness of the movements of both the upper and lower parts of the face—lower neuron type. With a supranuclear lesion, the weakness is only marked in the lower part of the face. A loss of emotional expression while voluntary movement remains good indicates a thalamic lesion as the cause of the weakness.

A lesion of the fifth nerve gives rise to both motor and sensory symptoms. The motor symptoms are shown by weakness in closing the jaw, and deviation of the jaw to the paralysed side on opening the mouth. Sensory involvement is shown by anæsthesia over one or all of the divisions of the fifth nerve on the face and mucous membrane of the mouth and nose, and by abolition of the corneal reflex.

The eighth nerve consists of two parts : the cochlear, concerned with the appreciation of sound ; the vestibular, concerned with the sense of position of the body in space. A lesion of either part of the nerve is rare in childhood, and a defect of hearing is most commonly due to an affection of the middle ear.

The ninth nerve supplies sensation to the palate, and taste to the posterior third of the tongue, and affection of the nerve will interfere with the palatal reflex.

The tenth and eleventh nerves supply the palate, the pharynx, the larynx, the sterno-mastoid and the trapezius muscles. An active palatal reflex in association with a paralysis of the palate on phonation is indicative of an upper motor neuron lesion, and occurs in association with a bilateral hemiplegia or diplegia. Such children, in the early years, often have some difficulty in swallowing, especially solid food.

The twelfth nerve supplies the tongue. A supranuclear lesion gives rise to weakness of the tongue, so that on protrusion it deviates towards the paralysed side, but there is no wasting of the intrinsic muscles.

THE MOTOR SYSTEM.—Inspection of the muscles of the limbs and trunk is undertaken to discover the presence of any weakness, wasting, or hypertrophy. It should be remembered that muscular tenderness can be elicited before wasting becomes evident in a weakened limb in cases of poliomyelitis. The state of the spinal muscles is tested by observing if the child can maintain the body upright and steady when in a kneeling position on a hard surface, and by arching the trunk forwards when lying on the back. Movements of the chest-wall and abdomen on forcible breathing indicates the state of the intercostal muscles and the diaphragm. When the diaphragm is intact and the intercostals paralysed, there is marked flaring of the costal margin. When the child makes an effort to raise itself to a sitting position, a movement upwards or downwards of the umbilicus indicates a weakness of the lower or of the upper segments of the abdominal muscles.

Muscular *hypertonicity* commonly occurs with lesions of the upper neuron, and in cerebral disease affects both the arm and the leg, as in hemiplegia and diplegia. *Hypotonicity* is produced by damage to lower motor neurons, and is also a characteristic symptom of cerebellar disease.

Notice should be taken of any tendency to *tremor*. Intention tremor is most often met with in cerebellar disease. Choreic movements are indicative of loss of cerebral control. Athetosis is a manifestation of cerebral disease, probably most often due to a lesion of the basal ganglia. Tremulousness or titubation on exertion is sometimes a symptom of the pre-paralytic stage of poliomyelitis.

Particular attention should be paid to any peculiarity of the *gait*. A staggering or lurching gait is indicative of a cerebellar lesion, while a disinclination to walk, because of pain, may be one of the earliest signs of spinal caries.

THE SENSORY SYSTEM.—In the young child it is not possible to test all the various forms of sensation. The appreciation of pain by pin-prick is practically the only one that can be examined.

The reflexes.—The *arm-jerks* are not always easy to obtain in children, but if the jerks on one side are much more active than upon the opposite side, there is an indication of a pyramidal lesion, as for example in hemiplegia.

The *abdominal reflex* is not present in young babies; it generally develops between the second and sixth months of life and is usually active after the fourth month. Its absence in any of the four quadrants of the abdomen in a case of poliomyelitis is a sign of paralysis of one or other of the abdominal muscles. In cerebral diplegia and bilateral hemiplegia, present at birth, or arising soon after birth, the abdominal reflexes are generally found to be active, and, again, in most cases of infantile hemiplegia the abdominal reflex is as active on the paralysed as on the sound side.

Fig. 344.—Extensor Plantar Reflex.

The *cremasteric reflex*, like the abdominal, develops during the first year of life.

The *knee jerks* are present in babies at birth and may be said never to be absent except under pathological conditions. The site of election on which to strike the patellar tendon is just on the outer side of the mid-line of the leg. With infants, the observer will find the point of the forefinger the most suitable percussor. The knee jerks may be absent in various conditions independent of any disease of the nervous system. They are not infrequently absent in pneumonia, broncho-pneumonia, severe enteritis and other toxic conditions. Their presence or absence is to some extent an indication of the severity of the toxæmia.

The best method of eliciting the *ankle jerks* is to place the patient lying on the abdomen, flexing the leg at the knee and holding the foot at right angles to the leg. A tap on the Achilles tendon gives rise to a contraction of the gastrocnemius and soleus, and produces extension of the foot. The ankle jerks are usually absent when the knee jerks are also absent, but there are exceptions to the rule—peroneal atrophy of Charcot-Marie-Tooth.

The *plantar reflex* is tested by scraping gently with the nail along the outer side of the plantar surface of the foot. Normally, in children above two years of age the great toe is flexed. In infants, according to Babinski, the plantar reflex is extensor in type up to the time the infant commences to walk. At any age the decision depends largely upon the character of the movement. It is the *slow* extension of the big toe which is of important diagnostic value. Extension and fanning of the other toes of the foot is also suggestive of a pyramidal lesion. When such a lesion is of slight severity, the planter is often indefinite, and more positive signs are an exaggeration of the knee jerks and some degree of adductor spasm of the thighs.

The cerebro-spinal fluid.—The cerebro-spinal fluid is secreted by the choroid plexuses of the four cerebral ventricles by a process of selective filtration. From the fourth ventricle into the cisterna magna some is accommodated in the reservoir of the spinal subarachnoid space, but the main flow is up and over the surface of the brain. It infiltrates deeply between the gyri and is in communication with the pia-lined perivascular spaces of Virchow-Robin, but absorption takes place through the Pacchionian bodies penetrating the great venous sinuses. A reversal of the flow through the choroid plexuses can be induced by the intravenous injection of hypertonic saline. By the selective filtration of the choroid plexuses the proteins and antibodies of the blood are largely withheld, but their admission is increased in the presence of meningeal inflammation, whether produced by bacterial invasion or aseptically by the injection of foreign sera intrathecally.

Dandy and Blackfan reckon that the cerebro-spinal fluid is completely renewed four to six times in twenty-four hours; Mestrezat, six to seven times; Masserman suggests a total of 422 c.cm. in an adult per diem. The fluid acts as a water jacket to the brain and spinal cord protecting them against sudden displacement and alterations of intracranial pressure. Its own pressure is subject to the intracranial venous pressure, and some degree of a mixing ebb and flow movement is caused by the effects of vascular pulsation and respiration.

So much is to be learned from an analysis of the fluid in nervous disorders that some knowledge of its composition in health and disease is essential. The normal fluid is a clear colourless watery fluid, with specific gravity 1·0075; plasma 1·025 (Merritt and Fremont-Smith, 1937).

Pressure.—Levinson (1928) places the normal pressure of the cerebro-spinal fluid in the newborn at 15 to 80 mm. in a water manometer, in older infants and young children 40 to 80 mm., and in children over six to eight years at similar figures to adults. These, using the recumbent position, are according to Merritt and Fremont-Smith 70 to 80 mm. as normal, 180 to 200 questionable, over 200 high, abnormal, and very high over 400 mm.

Chemistry.—Chlorides, glucose and urea pass readily into the fluid, the calcium is roughly half that of the blood, whilst some other blood constituents, such as sulphates and phosphates, are present only in minute quantities under normal conditions.

	Plasma	*Cerebro-spinal Fluid*
Chlorides	569–623	695–762
Glucose	74–125	45– 85
Calcium	9– 11	5·7– 6·8
Protein	—	15– 45

(Figures in mgm. per 100 c.cm.)

Chlorides.

Normal figures, C.S.F. 720 to 750 mgm. per 100 c.cm.
(Greenfield and Carmichael.)
C.S.F. 695 to 762 mgm. per 100 c.cm.;
Serum chloride 569 to 623 mgm. per 100 c.c.
(Merritt and Fremont-Smith.)

Samson found the chlorides in early infancy and sucklings, 630 mgm. per 100 c.cm. and over, and 690 to 725 in healthy infants above suckling age.

The chloride percentage of the fluid usually shadows that of the serum. It is lowered by vomiting, and acetone bodies also will often be found in acute general infections (pneumonia clinically resembling meningitis), and in meningeal inflammation. In purulent and tuberculous meningitis a persistent reduction of the chlorides below 680 mgm. along with decreased sugar content is always found sooner or later. In the first few days of the acute stage of aseptic meningitis and of the encephalitides a slight fall of chlorides often occurs, but the normal percentage is soon regained. In acute pneumonia the fluid chlorides may be lowered as they are in the serum and in the urine. The decrease in the C.S.F. has chiefly been found in those cases of pneumonia with meningeal symptoms—meningismus or meningeal hydrops. In meningismus, the chloride fall in the fluid may be explained as a dilution due to increased meningeal permeability associated with a lowered serum chloride, but the factor giving rise to the meningeal symptoms remains obscure; possibly it is a sudden increase in total quantity of cerebro-spinal fluid. In cases of pneumonia, however, without meningeal symptoms, the chlorides may be normal or even raised and the sugar content in all cases is commonly at a slightly raised level.

Very high chlorides, 800 mgm., are found in the fluid in the terminal stage of uræmia.

Glucose.—The percentage in normal fluid is 45 to 85 mgm., 30 to 70 mgm. in the newborn. An average fasting percentage for glucose in the fluid is 65 mgm., non-fasting 50 to 100 mgm.; in the serum 74 to 125 mgm. (Merritt and Fremont-Smith). In meningitis the glucose is utilized by the invading organisms or broken down by glycolytic ferments produced by inflammatory cells invading the meninges, as may happen even in the initial stage of aseptic meningitis. In purulent meningitis the sugar percentages in fluid and blood bear no relationship to one another (Greenfield and Carmichael).

A raised sugar content is found sometimes in the encephalitides—epidemic encephalitis—and in many general diseases, such as pertussis, smallpox and mumps.

Calcium has been found to average 6·22 mgm. per 100 c.cm. between limits of 5·7 and 6·8 mgm. (Critchley and O'Flynn); serum figures being

9 to 11 mgm. per 100 c.cm. Low figures are found in tetany and have been described in chorea (Warner, 1930).

Total protein in normal fluid is 15 to 45 mgm. per 100 c.cm. with average of 29 mgm. Samson gives higher figures for the healthy newborn, 40 to 80 mgm.; those for older children, 16 to 24 mgm. The amount is slightly greater in the lumbar sac due to stagnation than in the basal cisterns or ventricles; in children the ventricular percentage is 10 to 16 mgm.; cisternal 16 to 20 mgm.; lumbar 16 to 24 mgm.

The protein content in meningitis often rises as far as 200 mgm., due to transudation of serum through inflamed vessels, also in polyneuritis, poliomyelitis, and cerebral tumours; when a spinal block is present the lumbar protein may reach 7,000 mgm.

White cells in the normal fluid are usually 1 to 3 per c.mm. and are small lymphocytes; counts over 3 to 5 are suspicious or abnormal. In the healthy newborn, Samson puts the average at $3\frac{1}{2}$ and usually below 10, Waitz (1928) 6 to 20, and Stewart (1928) 20 to 30 per c.mm. It is not always easy in the newborn or at other ages to decide whether *red cell* admixture is *essential* or *accidental*, as the rich supply of veins in the vertebral canal is so easily damaged by the needle. On spinning a contaminated fluid soon after a faulty lumbar puncture the supernatant fluid is colourless (see discolouration), but it is yellow when the bleeding —essential—has occurred some time previously. Some red cells may be found in the fluids of infants born normally, and their presence has been estimated to occur in about 10 per cent. of births. As evidence of intracranial vascular damage, Sharpe and Maclaire (1925) state that blood and an increased protein content together are important, but not red cells alone. Roberts found a slight to heavy admixture of red cells in 14 per cent. of cases punctured within twenty-four hours, and only a third of those affected showed immediate symptoms of cerebral disturbance.

Polymorphs in the fluid suggest purulent meningitis, but a few may be present in the acute phase of poliomyelitis, and of the aseptic encephalitides. A moderate increase of cells, polymorphs and lymphocytes, from 5 to 250 may be present in the fluid in cases of inflammation of the cerebral sinuses and cerebral abscess, and when a cerebral tumour impinges on a ventricle a moderate pleocytosis may be seen but is usually confined to lymphocytes. At a figure of 300 cells per c.mm. polymorphs commonly give rise to turbidity, whilst lymphocytes up to 500 may be present in a clear fluid (Greenfield and Carmichael).

Discolouration.—Xanthochromia, a yellow colour of great variability, partly due to bilirubin, has been found in the fluid of the newborn by various authors, but more markedly in the premature than in full-term infants. In the latter Samson always found a yellow colour of the fluid in the first eight days. The deepest staining was found in jaundiced infants, but the yellowness disappeared from the fluid within a week. Roberts obtained a yellow staining without exception in 400 lumbar punctures in negro infants within the first fourteen days of life. Garrahan only found it in thirty out of 177 children.

At later ages a yellowness with a raised protein is found in poly-

neuritis, in cases of tumour impinging on a ventricular wall, especially in the posterior fossa, and in subarachnoid hæmorrhage following breakdown of the red cells when the discolouration may persist for as long as three weeks. The syndrome of Froin consisted of xanthochromia, excessive protein with massive coagulation, and pleocytosis of lymphocytic type. More commonly the term is now used for excessive protein often accompanied by yellow discolouration, as in the fluid below the level of a spinal block by tumour, or spinal caries.

In spinal block, by tumour for example, an indication of partial or complete obstruction can be obtained by means of Queckenstedt's test during lumbar puncture. Normally, light pressure over the jugular veins will cause the fluid to escape more forcibly; a negative test implies obstruction at some point in the spinal subarachnoid space.

In the following tables the composition of the cerebro-spinal fluid is set out, both in its normal and in some pathological states.

NORMAL COMPOSITION.

Clear, colourless	
Total protein	0·015–0·03 per cent.
Chlorides	0·72 –0·75 ,, ,,
Sugar	0·05 –0·06 ,, ,,
Cells	0 –3 per c.mm., lymphs.

Tuberculous meningitis.

Colourless, fine cobweb-like fibrin coagulum.	
Total protein	0·05–0·25 per cent.
Chlorides	0·7 –0·5 ,, ,,
Sugar	diminished
Cells	mainly small lymphocytes, sometimes polymorphs in early stages.
Micro-organisms.	Tubercle bacilli may be found in centrifuged deposit.

Acute meningitis (pyogenic).

Yellowish or greenish, with coagulum.	
Total protein	0·05–0·5 per cent.
Chlorides	0·7 –0·65 ,, ,,
Sugar	diminished or absent.
Cells	great increase, polymorphs.
Micro-organisms.	Usually present in stained smear from deposit, but cultural methods may be necessary.

Acute polio-encephalo-myelitis.

Colourless, fine cobweb-like fibrin coagulum.	
Total protein	0·05–0·2 per cent.
Chlorides	normal
Sugar	normal
Cells	excess of polymorphs at onset, later predominance of lymphocytes.

Epidemic encephalitis.

Colourless, no coagulum.	
Total protein	0·015–0·04 per cent.
Chlorides	normal
Sugar	normal or raised
Cells	5–100, lymphocytes.

In a suspected case of meningitis, besides examining the fluid for cells and the presence of organisms, it is essential to estimate the chloride and glucose percentages. The chlorides and glucose are diminished in all forms of bacterial meningitis, but not in other nervous diseases. A fall in the chlorides may be noted in acute lobar pneumonia, but the fluid is otherwise normal. Also in cases of cerebral tumour the chlorides may be diminished to 0·7 to 0·69 per cent. and the protein raised. This alteration in a clear fluid has sometimes led to a case of cerebral neoplasm being mistaken for an early case of tuberculous meningitis. Tuberculous meningitis and uræmia may clinically simulate one another closely, but in the latter the chlorides of the spinal fluid are normal or raised.

METHODS OF EXAMINATION.

Lumbar puncture.—With the patient fully flexed and lying on the left side, the point of the needle is inserted into the theca between the third and fourth, or fourth and fifth, laminal arches in the midline. A line joining the highest parts of the two iliac crests passes across the fourth lumbar spine. A fine needle should be used. Fluid is reached at a depth in the premature of 1½ to 2 cm., 2½ cm. in full-term infants, and in the second year up to 3 cm.

Cisternal puncture.—This method was introduced in 1919 by Ayer and is performed by tapping the cisterna magna with a lumbar puncture needle through the occipito-atlantoid ligament. The patient reclines on the left side as for lumbar puncture and care is taken to see that the vertebræ lie perfectly level one to another without any lateral curvature. The point of the needle is inserted through the skin just above the spine of the axis vertebra, and gently passed upwards and forwards in the same plane as a line joining the glabella, external auditory meatus, and spine of the axis. It is best at first to aim slightly higher so as to strike the base of the occiput. At a distance of 3 to 4 centimetres from the surface fluid should be reached. In piercing the occipito-atlantoid ligament a slight " give " is usually felt. The needle used should always contain a stylet. This method in conjunction with lumbar puncture is specially useful for diagnostic purposes in cases of suspected spinal block, *e.g.* tumour. A comparison is made between the samples of fluid taken from above and below the site of blockage.

Ventricular puncture. –In early infancy with wide patency of the anterior fontanelle, fluid can be obtained from the lateral ventricle. The needle is inserted in the lateral angle of the fontanelle, and passed downwards and slightly outwards to tap the ventricle. The sharpened end of the needle should be short, and will be less likely to do damage to veins. This method should never be used except in severe cases of meningitis when spinal drainage is ineffective, or for purposes of localizing the site of obstruction in cases of hydrocephalus.

Lumbar, cisternal, and ventricular puncture have therapeutic uses as well as diagnostic. In the treatment of meningitis penicillin or streptomycin can be introduced into the thecal space.

In cases of suspected spinal block, the cisternal route is chosen for the injection of lipiodol, which on X-ray examination helps to determine the upper limit of compression of the cord.

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HYDROCEPHALUS

Hydrocephalus, or the abnormal accumulation of cerebro-spinal fluid within the skull, is not in itself a disease but a secondary effect due to interference with the circulation or absorption of the fluid. Causes operative in its production are inflammatory, traumatic (hæmorrhagic), and developmental. Cerebral tumour gives rise to obstructive hydrocephalus by causing a block at some point in the ventricular pathway.

To understand the mechanism whereby hydrocephalus is produced, it is essential to know something of the source, flow, and absorption of the cerebro-spinal fluid, details of which are given briefly on page 1203.

Efforts to distinguish in infants between congenital and acquired types of hydrocephalus are often arbitrary, as some of the causes of hydrocephalus coming on after birth may have been in existence antenatally. Forking of the aqueduct of Sylvius, with two undersized tortuous channels, was found by Russell to be the common developmental defect. Hydrocephalus is a frequent accompaniment of congenital toxoplasmosis. A frequent natal and postnatal cause is meningeal fibrosis, secondary meningeal inflammation or hæmorrhage. In older children neoplasms in the region of the iter of Sylvius are chiefly responsible.

Site of obstruction in acquired hydrocephalus.—After a hæmorrhage or meningitis, the commonest situations for obstruction to occur are at the foramina of exit of the fourth ventricle, the cisterna magna, and in the narrow space between the free edge of the tentorium cerebelli and the brain-stem. The formation of adhesions at any of these localities will prevent the fluid from reaching the absorptive areas on the surface of the brain. According to Dandy's classification, the hydrocephalus is "obstructive" when the block is at some point in the ventricular system, and "communicating" when the arrest occurs outside the ventricles in the subarachnoid spaces, as for instance at the free edge of the tentorium cerebelli. Ventricular dilatation occurs in both types.

An "external" hydrocephalus, meningeal hydrops, due to increased formation of cerebro-spinal fluid or interference with absorption over the vertex, possibly to both causes, but without ventricular block or dilatation, occurs evanescently in meningismus, and for a longer period occasionally leading to optic atrophy in otitic and "toxic" hydrocephalus.

Symptomatology.—The characteristic feature of hydrocephalus in infants and young children is the enlargement and spherical shape of the head which may take place very rapidly, expanding to a circumference of twenty-two to twenty-six inches. At this age the cranial sutures are easily separated, and the anterior fontanelle can be widely open, almost from ear to ear. The cranial bones undergo pressure atrophy with the production of craniotabes. The bulging forehead overhangs the eyes, which are displaced downwards by depression of the orbital plates. Only the upper rim of the iris may be visible like a setting sun above the lower eyelid, and the infant may learn to pull down the eyelids in order to see. Nystagmus and strabismus are often present and pressure atrophy of the optic nerves is liable to occur and may lead to blindness.

Fig. 345.—Chronic Hydrocephalus: Photograph of a Child with so much Downward Displacement of the Eyeballs that Vision was only possible by Pulling Down the Lower Lids: this Action the Child had Learned to Perform.

(Photograph kindly supplied by Mr. Templeton.)

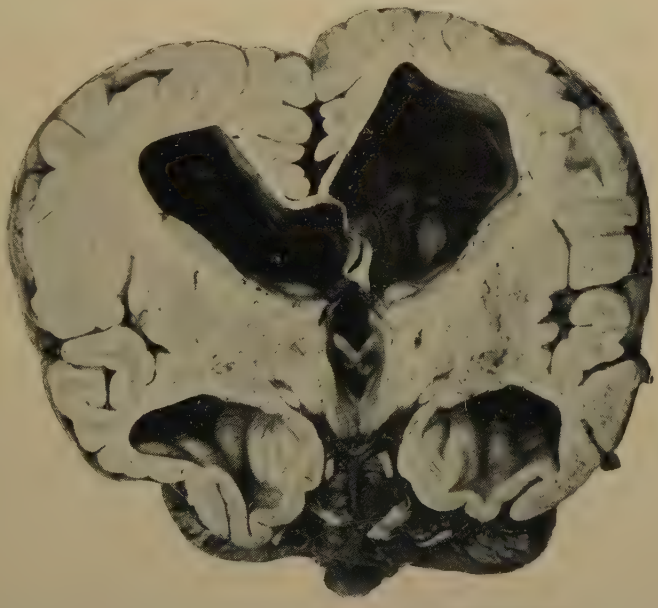

Fig. 346.—Hydrocephalus as the Result of Meningococcal Meningitis.

Note the dilatation of the lateral and third ventricles. In this case the block occurred in the region of the fourth ventricle

Signs of active progression are increasing girth of the skull, a constantly bulging fontanelle, conspicuous swollen veins in the parieto-temporal region, restlessness, screaming and vomiting. The limbs may become rigid, with increased tendon jerks and extensor plantars. The infant becomes emaciated and pines away. Hydrocephalus may occur in association with spinal meningocele either before or after operation on the spinal deformity; the cerebral as well as the spinal deformity being results of a developmental anomaly (see spina bifida).

Less severe cases may show no symptoms such as vomiting and paralysis, and the condition may become spontaneously arrested. With but slight enlargement of the head, the condition may be confused with rickets. In rickets, however, the head tends to be of a square shape with a flat vertex. The after-development of the child with hydrocephalus may proceed normally, but in other cases some mental impairment is usually noticeable, and a spastic ataxic condition of the limbs is often permanent.

Pathology.—In internal hydrocephalus, the hemispheres may be represented by a mere shell of tissue. The ventricular enlargement encroaches upon the white matter, while the cortex remains relatively intact, which helps to explain the fair amount of intelligence presented by many hydrocephalics in later life.

Procedure for localizing the site of obstruction.—An indication whether the hydrocephalus is obstructive in type or communicating, may be obtained by lumbar puncture. A large quantity of fluid obtained under pressure would signify free communication between ventricles and subarachnoid space—communicating hydrocephalus. This method, however, is not always reliable.

More exact information is obtained by the method of Dandy and Blackfan. Using neutral phenol-sulphone-phthalein as an indicator, 1 c.cm. of the solution is injected via the anterior fontanelle into one or other lateral ventricle. Lumbar puncture is then performed at intervals five and thirty minutes later. The escaping fluid is caught in a test tube containing a few drops of 25 per cent. solution sodium hydrate. Presence of the indicator substance is recognized by the cerebro-spinal fluid turning pink in the test tube. Early appearance of the indicator in the spinal fluid signifies that the ventricular foramena of exit are unobstructed, and therefore denotes a communicating hydrocephalus. Delayed appearance or absence of the colouring substance points to obstructive hydrocephalus.

In obstructive hydrocephalus the exact situation of the obstruction can be disclosed by *ventriculography*. The method entails the replacement by air of the ventricular fluid. Skiagrams will then reveal the level in the ventricles at which the air is obstructed.

Treatment.—Medicinal therapy is useless. Various surgical procedures have been attempted for the relief of obstructive hydrocephalus, but usually without success. These include excision of the choroid plexuses of the lateral ventricles and removal of the floor of the third ventricle. The most hopeful cases have been those with obliteration of the foramina

[illegible] [illegible] [illegible] [

1942, in the Royal Hospital for Sick Children, Glasgow, Fleming gives the primary lesion as pulmonary in eighty, abdominal in six, and undetermined in fourteen. Less often the meningeal involvement is secondary to tubercle of the joints, bone or middle ear. Droplet infection from contact with adults, adolescents, or older children, with open pulmonary tuberculosis is therefore the chief cause, giving rise to a primary complex in the lung of the child with secondary meningeal involvement. The history of contact can often be obtained among the relatives or others inhabiting the same house. Measles and whooping cough, indirectly, play an important part, as both are debilitating diseases and give rise to inflammation of the mediastinal lymphatic glands.

FIG. 347.—TUBERCULOUS MENINGITIS.

Photograph of a child during the later stages of the disease. The left hand was in constant movement, and only a blurred image of it appears in the photograph.

SYMPTOMATOLOGY.—The onset is usually slow and insidious. Often after a prodromal period of being out-of-sorts, the earliest definite symptoms are headaches, irritability, loss of appetite and vomiting. The child wishes to lie down, curled up on its side, dislikes the light, and from time to time may cry out with the pain in the head or on being disturbed. Stiffness of the neck, and pain on flexion of the head forwards is a most important sign, and should always be looked for. The presence of Kernig's sign may also be sought.

Gradually the child passes into a drowsy condition from which in the later stages it can only with difficulty be roused. Brief returns to full consciousness may occur, but are soon succeeded by relapses into stupor. Tremor of the limbs and twitching of muscles are often seen. These may be unilateral and disappear after a few days, giving place to the general rigidity which is common in the terminal stages of the disease. Convulsions may occur as an early symptom, but are more common in the later stages, partial rather than generalized. The head often is slightly retracted. Emaciation progresses rapidly, and the abdomen assumes a scaphoid contour. Constipation is usual throughout the illness.

The temperature presents no characteristic feature, but is generally raised 1° or 2° F. in an intermittent fashion, rising steeply at the terminal phase. In the first week of definite symptoms the pulse rate is often accelerated, slow in the second week, and increasingly rapid in the third week. From the appearance of the first definite symptoms to the fatal termination in the untreated case the usual duration is about three weeks.

The ocular symptoms are most variable, but paralysis of an external rectus muscle, giving rise to an internal strabismus, is the commonest.

Paralysis of the seventh nerve is sometimes seen. Swelling of the discs is frequently present in the later stages. Choroidal tubercles, if expressly searched for, are discovered frequently, being more common where there is evidence of miliary spread.

Tubercle bacilli can usually be found in the cerebro-spinal fluid, though not always in the first or second examination. The fluid is most often clear, colourless, with a cobweb-like clot on standing. Occasionally it is slightly turbid, or may be yellowish, if adhesions have occurred in the region of the cisterna magna sealing off the cerebral from the spinal fluid. In tuberculous meningitis the sugar content of the fluid is constantly reduced, cells, predominantly lymphocytic, are increased up to 300 per c.mm., and the protein is raised up to 200 mgm. Less attention is paid to the chlorides than formerly; a polymorphonuclear leucocytosis is usually present in the blood.

Morbid anatomy.—The cerebral convolutions are flattened and pale, and the Sylvian fissures are usually matted together. Some greenish lymph is generally present around the optic chiasma. Fine scattered tubercles are most plentiful on the dorsal surface of the cerebellum, and along the course of the great vessels on the surface of the brain. The membranes of the spinal cord are almost always involved in tuberculous meningitis.

On section, some dilatation of the ventricles is commonly present, and it is not unusual to find tuberculomata, varying from the size of a pea to that of a hazel-nut, scattered about in the cerebral substance. These have generally during life given rise to no symptoms (fig. 348).

Diagnosis.—In infancy, the early symptoms are sometimes attributed to "teething," a diagnosis to be avoided except after most careful consideration. In cases of sudden onset there is apt to be confusion with such conditions as acute pyelitis, pneumonia and the virus forms of meningo-encephalitis. With a sudden onset in the last a pleocytosis is often accompanied by a short-lived reduction of chlorides, even of glucose, which, however, soon readjust themselves to normal figures within a few days. The onset of uræmia in a patient having no history of an acute attack of nephritis may resemble tuberculous meningitis, but the urine contains albumin, the blood pressure is raised, and the area of cardiac dullness is commonly enlarged. Cases with spinal block at the cisterna magna and a yellowish spinal fluid may assume a typhoid-like state with tumid abdomen, but the Widal reaction is persistently negative and neck stiffness ultimately appears. Rare cases closely resemble cerebral tumour with nystagmus, strabismus, early papilloedema, increased tendon reflexes, and normal chloride and sugar percentages in the fluid up to six weeks, but the latter ultimately fall progressively away. Very occasionally at the start a tuberculous meningitis excites a neutrophil reaction in the fluid, and, if the culture is sterile, doubt exists whether tubercle bacilli or pyogenic organisms are responsible. In this contingency it is best to give sulphonamides without waiting, as they cannot harm a tuberculous and may save a meningococcal patient.

Prognosis.—Before the advent of streptomycin the disease was, with

very rare exceptions, fatal. Cases reported with definite presence of Koch's bacillus in the fluid and " recovery " are to be accounted for as temporary remissions in the course of the disease. Martin reviewing 2,166 cases diagnosed as tuberculous meningitis in hospitals in London and Vienna found that one per cent. represented the cases discharged as cured or relieved. Cramer and Bickel collected from the literature forty-five authentic cases with apparent cure. The percentage of reported recoveries

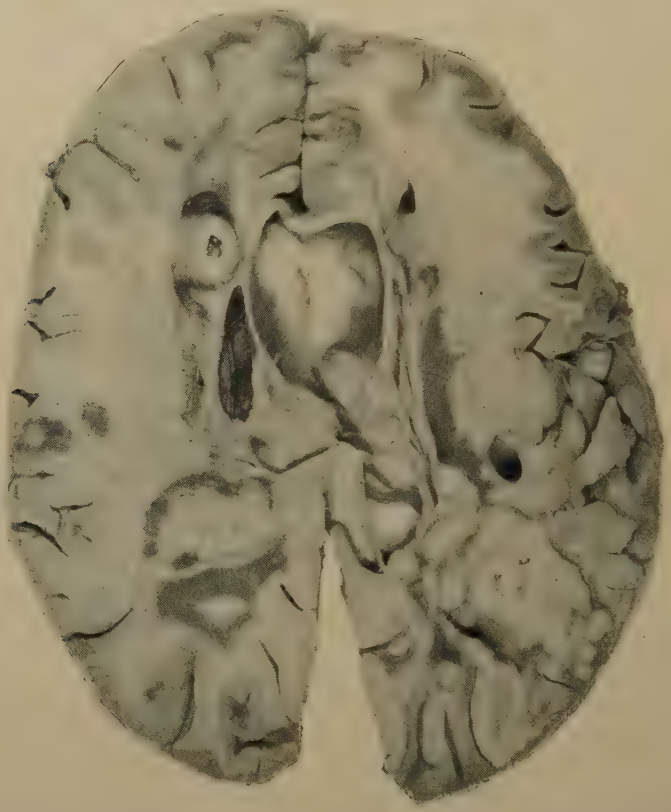

FIG. 348.—HORIZONTAL SECTION OF BRAIN, SHOWING LARGE TUBERCULOUS MASSES EMBEDDED IN THE SUBSTANCE OF THE HEMISPHERES.

The child died of tuberculous meningitis.

at different age periods is smallest in the early years of life, but in most cases of reported recovery the period of survival is too short for them to be accepted as cured beyond doubt. A period of eighteen months has been recorded, but in the majority much shorter periods are mentioned. It is possible that a tuberculoma situated near the surface of the brain or ventricles can leak a few tubercle bacilli temporarily into the cerebrospinal fluid, and for a considerable interval to elapse before the onset of the fatal meningitis. It must be accepted, however, that rare instances of recovery do occur. With the introduction of streptomycin an overall

recovery rate of some 30 per cent. is being achieved, whilst in some centres the results are better than 50 per cent. It is too soon to know what the remote results will be.

TREATMENT.—Streptomycin is the antibiotic responsible for the survival of a variable proportion of cases of tuberculous meningitis. It is usually given intrathecally in doses of 50 mgm. below the age of three years, and 100 mgm. above this age. Various rhythms of administration have been tried (Rubie and Mohun, MacCarthy and Mann), and the present tendency is to give it daily for longer and longer periods, or until the fluid has returned to normal (Smith and Vollum, Pasquinucci). Streptomycin is also given intramuscularly at the same time, in doses of 20 mgm. per lb. of body-weight per day given twelve-hourly (M.R.C. Report, 1948) for six months or longer.

It is not known why a proportion of apparently favourable cases do not respond to treatment, and in trying to improve the results various sulphones (Cocchi), tuberculin (Smith and Vollum) and streptokinase have been added to the therapy. It is still too early to evaluate the part played by these. In addition, as para-aminosalicylic acid appears to hinder the appearance of streptomycin-resistant strains of tubercle bacilli, this is often given orally. Daily high doses of vitamin A are also given by Cocchi.

Apart from these drugs, general supportive measures are used. Raised intracranial pressure may be relieved by ventricular drainage, which in the case of young children may be carried out through the fontanelle and in older children may be done through an indwelling catheter inserted direct into the ventricle through a burr hole in the skull. The greatest caution should be used in trying to relieve pressure by lumbar drainage, owing to the danger of allowing the brain stem to be forced into the foramen magnum and producing a mechanical block.

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Meningococcal meningitis (cerebro-spinal or spotted fever).—The *Neisseria meningitidis* was isolated by Weichselbaum in 1887. By means of agglutination tests Gordon (1917) separated the infective agent into four groups, types I, II, III and IV. Types I and II account for the majority of cases and have about an equal prevalence. Type II is said to be commoner in *posterior basic meningitis*. Meningococcal meningitis occurs sporadically and in epidemics, infection being spread by carriers, temporarily by those suffering from the disease and chronically by others with an apparent immunity. Overcrowding and frequent mixing of the

population in an infected area as specially occurs in war time are important factors in the production of an epidemic.

The meningococcus enters by the nasopharynx and produces a blood infection with subsequent invasion of the ventricles probably through the plexuses, causing a choroido-ependymitis and secondly a meningitis. The possible manifestations of meningococcal infection are as follows :

Septicæmic { Meningococcal adrenal syndrome
Septicæmic (fulminating, acute and chronic)

Meningo-encephalitic { Meningeal
Meningo-encephalitic
Mixed encephalitic-adrenal

The meningeal type, or cerebro-spinal fever, is the commonest and the one which will be principally discussed. The pure adrenal syndrome and

Fig. 349.—Child with Acute Meningococcal Meningitis, showing Marked Retraction of the Eyelids and Staring Appearance of the Eyes, often associated with Blindness.

Compare the position of the eyes with the downward displacement seen in hydrocephalus (fig. 345).

mixed encephalitic-adrenal as described by Banks and McCartney (1943) give (1) an acute onset, fulminating septicæmia, purpuric rashes, weak pulse, pallor, cyanosis, vomiting and mental condition clear to termination, often fatal within twenty-four hours ; (2) acute onset, fulminating septicæmia, purpura, weak pulse, cyanosis, coma and stertorous breathing. In the second group at autopsy are found adrenal lesions and purulent meningitis, focal encephalitis and perivascular hæmorrhages.

Meningococcal septicæmia may be fulminating, acute or chronic, and the two later may be followed by meningitis. The symptoms are fever, shivering or rigor, general aching and headache, purpuric, skin lesions, and localized joint and muscle pains. A neutrophil leucocytosis is usual in meningococcal infection and reaches high figures, 20,000 per c.mm. and over in the septicæmic type. The meningococcus can usually be recovered on blood-culture, if several attempts are made.

Cerebro-spinal fever, or meningitis, occurs at all ages, is rare in the first three months, but three-quarters of the sporadic cases are in children under ten years of age. The onset is acute or subacute with headache, aching pains, shivering, fever 101-104° F., stiffness of the neck, muscular stiffness, Kernig's sign, twitchings, cutaneous hyperæsthesia, delirium or stupor. Rashes, petechial, purpuric or herpetic, appear about the commencement of meningeal signs in 10 to 15 per cent. of cases. Ocular lesions, strabismus, amaurosis usually temporary, occur, but deafness is a more common symptom and may be permanent. Arthritis is a complication of some cases but usually clears up. In severe cases at autopsy, besides purulent meningitis, there may be found in the substance of the brain foci of œdema, capillary thromboses and hæmorrhages—meningo-

FIG. 350.—MENINGOCOCCAL MENINGITIS DURING THE CHRONIC STAGE, SHOWING MARKED RETRACTION OF THE HEAD, OPISTHOTONOS, AND CONTRACTION OF THE LIMBS.

encephalitis. Similar lesions or severe toxic disturbances can occur in cases which recover. For example, a boy of eight years within twenty-four hours from the onset of illness lost the use of one arm completely and of the other partially. Some wasting became obvious, but within six months full recovery of power and size of muscles had occurred. An initial bacteriæmia ascertained by blood-culture has been found in 25 to 30 per cent. of cases by Craster and Simon (1938). Meningococci by suitable staining in the cerebro-spinal fluid are seen both within and without the leucocytes and cultures on enriched media reveal the characteristic kidney-shaped paired cocci. For changes in the cerebro-spinal fluid, see under purulent meningitis.

Post-basic meningitis was shown by Still to be an attenuated form of meningococcal infection. It occurs in the first six months of life and has its greatest seasonal incidence in late winter and early spring. The onset

is an insidious passage from not gaining weight, apathy, vomiting, fever, and possibly convulsions to a state of increasing head retraction, opisthotonos with rigid extension of the limbs, fixed staring eyes with retraction of the eyelids, emaciation, and attacks of screaming. A tense or bulging fontanelle is present except when vomiting is frequent. Vision sometimes appears to be completely lost, which is a striking feature of the condition. The amaurosis is often an early symptom and is not due either to choked disc or to optic atrophy. It will sometimes remain permanently after recovery otherwise has taken place, or it may persist for as long as

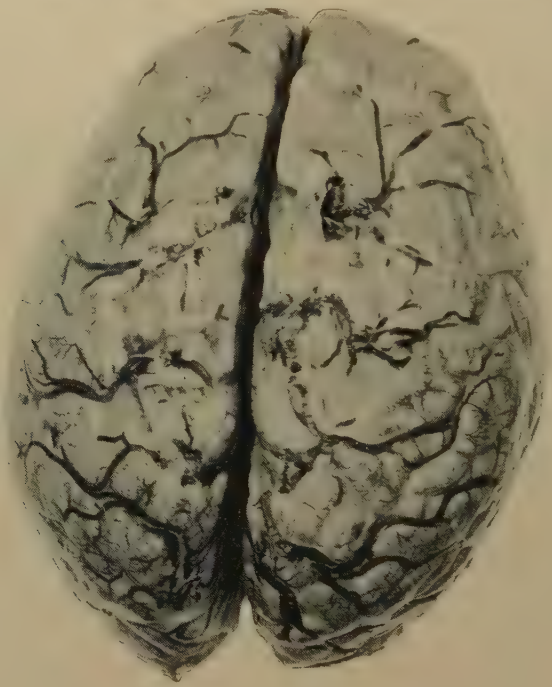

FIG. 351.—MENINGOCOCCAL MENINGITIS.

The whole vertex of the brain is seen to be covered with exudation, on which the dilated, congested and thrombosed veins stand out.

four months before vision is recovered. Hearing is usually acute or hyperacute. This symptom stands out in striking contrast to the deafness often found in the cerebro-spinal form of the disease. *Rashes* seldom occur in the post-basic type, but *joint swelling* is present in some cases, generally peri-articular rather than articular.

With the slow onset adhesions leading to hydrocephalus often have formed before treatment is started, and on lumbar puncture the diplococcus being a feeble strain may not be found, having died out.

PATHOLOGY OF MENINGOCOCCAL MENINGITIS.—Owing to the small degree of cellular reaction in the ventricles the meningococci multiply freely and it is not until they come into contact with the meninges that a

reaction is set up and they become ingested by cells of endothelial and blood origin (Greenfield and Carmichael).

In posterior basic meningitis the inflammation is most conspicuous at the base of the brain, especially around the base of the cerebellum and in the region of the fourth ventricle. The meningitis may extend forward so as to involve the optic chiasma, but as a rule it is much less in this region than in cases of tuberculous meningitis. In chronic cases in which internal hydrocephalus has developed, the ependymal lining of the ventricles often has a roughened, yellow, shaggy appearance.

In the cerebro-spinal type, the inflammation may spread over the whole vertex of the brain, and the surface of the hemisphere is seen to be covered with thick green pus, through which engorged veins stand out prominently. The spinal cord invariably shares in the meningeal inflammation, where as a rule it is most obvious on the dorsal surface of the cord in the cervical and lumbar regions, whilst the thoracic area remains fairly clear. The microscopical changes in the brain tissue itself are very slight, and the infiltration of the meninges is almost confined to the subarachnoid space.

Prognosis.—The mortality of meningococcal meningitis has been steadily reduced. Formerly when using antimeningococcal serum it fell from 50 per cent. and over untreated to about 30 per cent. Next on combined intravenous antiserum and sulphonamide by mouth to 11·8 per cent. (Banks, 1938). Excellent results are now obtained on sulphonamide therapy alone, with, for example, a gross mortality rate of 8·6 per cent. in a series of 500 cases recorded by Harries (1942). Penicillin has reduced this mortality still further.

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Streptococcal, pneumococcal, influenzal and staphylococcal forms, have in common the symptoms of acute meningitis, namely, headache of increasing severity, pains at the back of the neck and in the spine spreading into the legs on attempting movement, hyperæsthesia, vomiting, fever and convulsions. The onset is seldom so abrupt as in cerebro-spinal meningitis. The child resents being moved and lies curled up on its side. Signs of meningeal irritation are vomiting, cervical rigidity, Kernig's sign, and occasionally head-retraction ; delirium is often present at first but tends to give place to drowsiness, stupor, coma.

The *streptococcal* form occurs as a complication of otitis media, mastoiditis, less often of pneumonia, osteitis, erysipelas, paranasal and cavernous sinus inflammation. About 90 per cent. of all cases are due to hæmolytic streptococci ; meningeal infection by streptococcus viridans is rare. At the onset of meningeal invasion from an otitic source, the child may be drowsy or show signs of apprehension and increased mental activity. Sensations of cold, shivering, or an actual rigor, are common

with commencement of headache and vomiting. Often the otitis media, acute or chronic, has ceased to discharge.

The spinal fluid may show a cell count up to 20,000 polymorphs or more per c.mm., and in the most severe cases organisms may be plentiful and cells absent. At the beginning of meningeal infection via the dura mater the local inflammation gives rise to the presence of numerous cells in the fluid, organisms are usually absent and the sugar content is but little reduced—a condition of *serous meningitis*. In such circumstances the prognosis is naturally more hopeful, as a generalized meningitis has not yet developed.

The mortality from hæmolytic streptococcal meningitis at all ages used to be about 97 per cent. ; the results obtained with antistreptococcal sera were disappointing. Under sulphonamide therapy the mortality fell to about 30 per cent. (Sappington and Favourite, 1939), and to 15 per cent. (Kolmer, 1940). Neal and Applebaum in seventeen cases so treated, all secondary to disease of the ear or mastoid and with streptococci proved in the cerebro-spinal fluid, report recovery in thirteen, death in four. A hæmolytic streptococcal infection should respond either to sulphonamides or to penicillin. The less common non-hæmolytic viridans type of infection is susceptible to penicillin and usually not to sulphonamides (see treatment of meningitis).

The *pneumococcal* form is usually secondary to otitis media, pneumonia, empyema, tonsillectomy, or sinusitis, but can be primary. Primary cases occur at any age and even in the newborn of a few hours to a few days old, apparently in some instances being due to intra-uterine infection. The mortality used to be near 100 per cent. although instances of recovery were reported from time to time but usually in cases with mild symptoms and an organism of low virulence. Up to 1927 there were only 150 recorded cases of recovery from culturally proved pneumococcal meningitis (Goldstein and Goldstein).

With sulphonamides some successes were claimed about equally in the primary and secondary types, but the presence of a positive blood culture appeared greatly to lessen the chances of cure ; blood culture was positive in seven out of eight fatal cases ; only one positive blood culture in seventeen cases successfully treated with sulphonamides. Hewell and Mitchell gave records of thirty recoveries with chemotherapy in patients between five and forty-seven years of age. Pneumococcal meningitis is frequently resistant to sulphonamides and penicillin is more effective. Smith, Duthie and Cairns advocate the following treatment on detection of the pneumococcus : intrathecal and systemic penicillin and sulphadiazine by mouth. For an infant or child a lumbar injection of 2,000 to 10,000 units of penicillin (2,000 units per c.cm.) is given, and repeated once or twice at twelve-hour intervals according to the improvement seen in the fluid withdrawn, and thereafter daily lumbar injections for at least five days. The fluid is usually sterile after the second lumbar injection, but with any indication of the existence of an intrathecal block the penicillin must be injected, either cisternally, or by ventricular puncture through the fontanelle or cranial burr-holes. Systemic penicillin at 4,000 units per lb.

body-weight per diem is given by three-hourly intramuscular injections, or by a continuous drip, for four or five days to overcome the primary infection. Alternatively one of the depot penicillins may be given less frequently. Sulphadiazine by mouth ($\frac{1}{2}$ to 1 gramme four-hourly according to age of child) is given throughout and especially to tide over the period of withdrawal of the spinal penicillin, though, if poorly tolerated, it can be omitted during the period of intrathecal injections. The occurrence of fits in the acute stage in infants and young children must be controlled by phenobarbitone given intramuscularly if necessary. By this combined method it is hoped that the mortality of pneumococcal meningitis may be brought below ten per cent. Recent American experience of the use of aureomycin alone has been very favourable.

The *influenzal* form due to the Pitman type B of the *Hæmophilus influenzæ* can be secondary to otitis media or broncho-pneumonia, but is commonly primary. In 1899, Pfeiffer isolated the organism in pure culture from a case of meningitis in an infant of seven weeks. Huntington and Wilkes-Weiss (1936) found that 473 out of 500 reported cases were in infants under two years of age. They obtained sixteen positive blood cultures out of twenty-four cases in the initial stage. The invasion of the meninges is by the blood stream.

Symptoms may appear acutely or gradually, and in infants irritability, vomiting, drowsiness, fever, diarrhœa, may suggest a gastro-intestinal rather than a meningeal infection. In older children a prodromal period of sore throat, vomiting and headache is common before signs of meningitis are recognized. A blood count gives either a leucocytosis or a leucopenia, and the cerebro-spinal fluid shows cells, chiefly polymorphs, up to several thousands.

The mortality used to be 92 per cent. (Rivers, 1922), and in fifty recorded cases of recovery Jones (1937) found only four under one year of age. Aléman (1940) collected records of 82 cases treated with sulphonamides with ten recoveries, of which six were in children over two years of age.

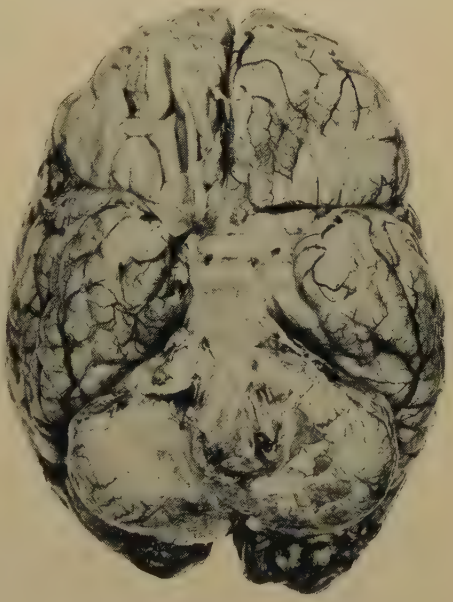

Fig. 352.—Influenzal Meningitis.

The base of the brain is seen to be covered with a thick exudation. The causative organism in this case was shown to be the Hæmophilus influenzæ.

Hæmophilus influenzæ has a variable degree of resistance both to sulphonamides, and penicillin. Within the last five years a great advance in the recovery-rate from influenzal meningitis, both in infants as well

as in older children, has been achieved with a combined therapy of sulphadiazine and type-specific antibody in rabbit serum. Alexander (1944) in a group of cases receiving controlled therapy reported 82 per cent. of complete recoveries. The dosage of antibody is assessed according to the sugar content of the spinal fluid. The antibody is given intravenously, 50 mgm. diluted with 100 c.cm. normal saline, over 50 mgm. in 200 c.cm. saline, administered in a period of under two hours.

Spinal fluid sugar mgm. per 100 c.cm.	Type-specific antibody mgm.
under 15	100
15–25	75
25–40	50
over 40	25

Subsequent requirements of antibody are determined by evaluation of the level of antibody in the patient's serum. Using rabbit serum and sulphonamide, Smith *et al.* (1946) report only two deaths and two instances of residual cerebral damage in 23 cases under two years of age.

It is advisable to begin treatment by giving daily systemic (200,000 to 500,000 units) and thecal (30,000 to 50,000 units) penicillin, and sulphadiazine or -thiazole by mouth or by intravenous drip until the susceptibility of the strain to one or other forms of therapy is proved by laboratory tests. Adequate hydration is maintained by intravenous drip. As influenzal meningitis has a tendency to relapse, it is advisable to examine the spinal fluid more frequently and the course of sulphonamide or of penicillin should be continued longer than in other types of meningitis. Recovery in apparently chronic cases is possible and disappearance of symptoms may be gradual. Streptomycin has also proved a valuable drug for this type, being given in the same dosage as for tuberculous meningitis. The emergence of resistant strains of *H. influenzæ* is common.

The *staphylococcal* form occurs as a rare complication of skin, or bone. or ear disease. Before chemotherapy, Michels and Gonne (1939) found records of eight recoveries. With sulphonamides some instances of recoveries have been claimed, but penicillin is to be preferred in staphylococcal meningitis. Laboratory tests for sensitivity should be made.

Purulent meningitis due to other organisms.—Köhler mentions the occurrence of meningeal infection in the newborn due to *Bact. coli*, *Friedlander's bacillus*, *Ps. pyocyanea*, *N. catarrhalis*, and the Koch-Weeks bacillus, infection probably occurring in the first few days of life. To this list can be added *Bact. fæcalis alkaligenes* and *Proteus*. Infection may arise from umbilical sepsis or from trivial scalp wounds. As many of these infections respond readily and completely to streptomycin a lumbar puncture should always be performed where the possibility of meningitis is entertained.

Meningitis due to the Salmonella group is rarely seen, and may be primary or secondary (Magreth, 1929), occurring as a complication of enteric fever in the third or fourth week. The spinal fluid remains clear or becomes slightly turbid, and lymphocytes predominate and are not usually numerous. The organism is stained by smear preparation, or

grown on culture. The mortality records vary from 50 to 100 per cent. A few recoveries are recorded in which chemotherapy was used, *e.g.* two of paratyphoid B meningitis by Patterson (1942).

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Penicillin and sulphonamides in the treatment of purulent meningitis.—Penicillin is claimed to have both a bacteriocidal and a bacteriostatic action. It is usually inactive against gram-negative bacilli, but the *Hæmophilus influenzæ* in some of its types may be susceptible to treatment. It is always desirable to carry out laboratory tests for sensitivity of the invading organism. Penicillin does not pass the blood-cerebro-spinal fluid barrier in any quantity of therapeutic value, but in elimination after thecal injection passes readily from fluid into blood. In infants and young children 5,000 to 20,000 units per intrathecal injection is a sufficient figure, except in influenzal meningitis when greater amounts are often necessary. Penicillin is specially indicated in staphylococcal and streptococcus viridans meningitis, and may be essential in hæmolytic streptococcal, pneumococcal and even meningococcal forms when either an acquired or a natural resistance to sulphonamides is ascertained. A combined therapy, penicillin and sulphadiazine, is specially recommended in pneumococcal and influenzal meningitis, as it has been shown that penicillin has a synergistic action with the sulphonamides. The part to be played by streptomycin remains to be finally determined, its drawback being the readiness with which some organisms become resistant to it. Insufficient data are yet available concerning the newer antibiotics, such as chloromycetin and aureomycin, but as they are said not to engender bacterial resistance and may be given by mouth it is likely in the future

that they will play a significant part in the treatment of some forms of meningitis. Aureomycin may also be given intravenously.

The sulphonamides are mainly bacteriostatic, but have some bacteriocidal action. Their chief effect is to arrest further bacterial growth until the natural defences of the body can overcome the invader. They do not neutralize bacterial toxins, or stimulate leucocyte activity or the production of antibodies. Though organisms vary in their sensitivity to one or other form of sulphonamide, the difference depends chiefly upon disparities in rate of absorption, concentration in the blood and cerebro-spinal fluid, and rate of secretion. This explains how with one form of sulphonamide or possibly as a result of insufficient dosage an organism may become drug-resistant, but may still be sensitive to another sulphonamide in adequate dosage and spinal-fluid concentration. Laboratory assessments of the sulphonamide content of the spinal fluid and of the sensitivity of the invading organism are necessary when adequate dosage produces no betterment within two or three days.

The comparative concentration in the cerebro-spinal fluid (Medical Use of Sulphonamides, M.R.C. War Memo., No. 10, 1943 and No. 10, 1945) of sulphanilamide is 90 to 100 per cent. of the blood figure, of sulphapyridine and sulphadiazine 50 to 70 per cent., and of sulphathiazole 15 to 40 per cent. (sulphadimidine 50 to 80 per cent.). Despite the lesser diffusibility of sulphathiazole into the C.S.F., 1·5 per cent. on a high dosage, Banks found it highly effective in meningococcal meningitis and it is of value in other forms of purulent meningitis. A particularly high blood concentration can be obtained with sulphadiazine owing to its slow excretion. Sulphapyridine is more slowly absorbed and more rapidly excreted. Sulphadimidine is quickly absorbed, reaching a high blood level, and its rate of excretion is lower than that of sulphapyridine. The lesser toxic effects, nausea, vomiting, cyanosis, and mental depression do not occur so much with sulphadiazine, sulphathiazole and sulphadimidine as with sulphapyridine and sulphanilamide. Renal damage, hæmorrhage and anuria due to crystallization of acetyl derivatives is most liable to occur using sulphapyridine, sulphanilamide and sulphadiazine. This event is seen less often in children than in adults, but steps to ensure proper hydration are necessary, 1,500 to 2,000 c.cm. of fluid daily, even by intravenous drip of saline or Hartmann's solution in infants. The solubility of sulphonamide is increased in alkaline solutions, therefore renal damage is less likely to occur if alkalis, such as potassium citrate and sodium bicarbonate 10 to 20 grains of each, are given by mouth with each dose of sulphonamide to render the urine alkaline.

Dosage is fairly uniform for the series, under three years a daily dose of 3 gm., from three to five years $4\frac{1}{2}$ gm., five to ten years 6 gm. for two or three days followed by a two-thirds daily dosage for two days and a one-third daily dosage for two more days (Banks). An initial loading extra dose of half to one gramme is added to raise the blood percentage rapidly. In critical circumstances, such as unconsciousness, one of the drugs is given by nasal tube or intravenously as a sodium solution $\frac{1}{2}$ to 1 gm. in 10 to 20 c.cm., but the intrathecal route must never be used,

as permanent nerve lesions have frequently been produced. Under suitable dosage the cerebro-spinal fluid can be made sterile in twelve to forty-eight hours. Lumbar puncture is done once for diagnostic purposes and once again to estimate concentration, but more often in influenzal and pneumococcal meningitis.

In streptococcal meningitis, as an additional therapeutic measure, concentrated antitoxin (Lederle) 5 to 10 c.cm. may be given intravenously or intramuscularly. In the meningococcal mixed or meningo-encephalo-adrenal syndrome, in addition to chemotherapy eucortone 4 to 5 c.cm. is given intramuscularly and repeated four-hourly if necessary.

Serous meningitis.—As a complication of acute or chronic middle-ear suppuration an arachnoiditis may be set up. "Serous meningitis" is the stage of early localized meningeal inflammation adjacent to the petrous bone, which precedes a generalized purulent meningitis. A raised irregular temperature with signs of meningeal irritation are present. The cerebro-spinal fluid is under increased pressure, clear, or rarely cloudy, and contains an increase of protein and cells chiefly polymorphs, and on culture organisms are absent, or only a scanty growth is obtained. The glucose content may be low, but the normal quantity of chlorides indicates that the meningeal reaction is *local* and not *generalized.* Treatment is by immediate operation for the relief of the middle-ear suppuration and administration of sulphonamides or of penicillin.

Other less common types of cerebral serous meningitis are "otitic" and "toxic" hydrocephalus. These conditions affect children and adolescents chiefly. The first is a complication of acute or chronic ear disease; in the second no primary septic focus is discovered or there has been a preceding coryza or tonsillitis. Apparently as a result of toxic irritation an excessive formation and possibly defective absorption of cerebro-spinal fluid occurs causing external hydrocephalus. Ventricular dilatation is said not to occur (McAlpine, 1937). Signs of intracranial hypertension in the otitic form soon develops either acutely with pyrexia and cervical rigidity, or more slowly and without fever; in the toxic type they have usually appeared gradually over a week or two, but without either pyrexia or neck rigidity. The symptoms in both are severe fronto-occipital headache, nausea and vomiting tending to occur only in the younger patients, the mental state usually remains clear, a high degree of papillœdema commonly develops, and as a result of the high intracranial pressure the plantar responses may become extensor. In the otitic type, Symonds states that a sixth nerve palsy on the side of the affected ear is common. That otitic meningitis and otitic hydrocephalus are related conditions is revealed by a case of Garland's, a girl of nine years, who presented the features of both conditions alternatively over a period of four months (Garland and Seed, 1936).

The spinal fluid in both conditions is under great pressure, over 200 to 300 mm. of water, but is clear and of normal composition. The absence of a raised protein and of a lymphocytic increase is against the presence of an abscess.

Treatment is by repeated lumbar tapping, two or three times a

week at first, until the initial pressure on lumbar puncture is about 120 to 150 mm. water. With high pressure the fluid must be drained slowly. A reduction of the degree of papillœdema is a sign of recovery. Inadequate spinal tapping may lead to permanent impairment of vision from the onset of optic atrophy. In the otitic form, myringotomy is often required and further operation is usually not necessary.

A spinal arachnoiditis, or *meningitis serosa circumscripta spinalis*, is an inflammatory process of obscure origin, whereby at some level of the cord, but usually dorsal or lumbar, opaque or milky strands and adhesions of the pia-arachnoid are formed, sometimes with encysted collections of fluid, producing signs of a compression paralysis. The clinical picture closely resembles that of spinal tumours, and a correct diagnosis is seldom made before a laminectomy is performed. In forty-one cases Elkington found the ages to be between twenty and seventy years; Hiller reported a case in a boy of eight years and Wyllie one in a boy of six and a half years.

The condition develops gradually over several years, seldom rapidly. Early symptoms are spontaneous pains unilateral or bilateral in the cutaneous distribution of several spinal segments, diminution of sensation below a certain segmental level, often of unequal degree on the two sides of the body and with separate levels for the different forms of sensation, dragging of the legs and muscular rigidity, and sphincter disturbance either urinary or fæcal. Spinal radiography usually shows no abnormality.

The diagnosis is suggested, as against one of spinal tumour, by the spontaneous root pains of different distribution at the onset, the inequality and dissociation of sensory disturbance on the two sides, and the chronicity before signs of severe compression of the cord is reached. A lipiodol examination commonly shows a fragmentation or "guttering" of the oil at the level of the adhesions, rather than a complete arrest as in the cases of spinal tumour. According to the degree of obstruction the lumbar fluid gives a normal or gross increase of protein, a few lymphocytes, and is usually colourless.

The prognosis depends on the degree of decompression that can be accomplished at laminectomy by severing adhesions and removal of encysted fluid, but in chronic cases recovery of function is prevented by secondary degenerative changes having developed within the cord.

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Meningitis leptospirosa.—This can occur in two forms, either in Weil's disease, spirochætosis icterohæmorrhagica, transmitted by contamination of food or water by the urine of infected rats (see p. 609), or as leptospirosis canicolaris, a spirochætal infection of dogs occasionally

transmitted to man (Campbell *et al.*). Cases of Weil's disease with meningeal signs are often anicteric (Buzzard and Wylie).

The clinical signs are fairly similar in both conditions, an abrupt onset, high fever, lasting about eight days, shivering and rigors, conjunctival suffusion, and signs of meningeal irritation. The kidneys are affected, and albumin and red cells are present in the urine. The cerebro-spinal fluid is under pressure with increased protein and cells, chiefly lymphocytes, but normal chlorides and glucose.

The leptospira of Weil's disease can be recovered from the urine or blood in the first six days of illness, and the leptospira of canicola fever from the blood and possibly the cerebro-spinal fluid during the first week. From about the seventh day, the serum agglutination reactions serve to distinguish the two conditions, and to differentiate them from lymphocytic meningitis and abortive poliomyelitis, which they may clinically resemble.

In either form of meningeal leptospirosis recovery can be expected, but chemotherapy with penicillin, streptomycin, or aureomycin is recommended.

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Mumps meningitis.—The virus of mumps is potentially neurotropic. Even in uncomplicated cases of parotitis and in contacts the cerebro-spinal fluid has frequently shown a high lymphocytosis. The commonest nervous complication of mumps is meningitis coming on about the fourth day and lasting for about a week, the symptoms being pyrexia, severe headache, vomiting; and facial paralysis, deafness, rarely optic neuritis, may also occur. Another complication is polyneuritis affecting all four limbs and coming on within a few weeks from the onset of parotitis. The nervous signs usually clear up entirely, but deafness may be permanent. A meningo-encephalitis, or a myelitis, are rare.

Fabian records three cases of mumps meningitis in children aged seven, six and four years, all occurring in the same epidemic. One child died. Feiling has reported a cellular count of 3,500 per c.mm., of which 96 per cent. were lymphocytes, and in a fatal case found venous congestion of the cortex and definite signs of meningitis at the base of the brain.

Treatment.—There is no specific treatment, but a daily lumbar puncture should be done during the acute phase.

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Acute aseptic meningitis and acute lymphocytic chorio-meningitis.—Acute aseptic (Wallgren, 1925), benign lymphocytic and epidemic serous meningitis have been the titles used to describe an acute illness of meningeal type usually of short duration and favourable outcome, and presenting a raised cellular and protein content in a bacterially

negative cerebro-spinal fluid. Children are chiefly affected and sometimes young adults. The syndrome may depend upon infection by viruses in all cases, but in only a third of the total has this been proved. Three types of virus are recognized: that of choriomeningitis, isolated by Armstrong and Lillie (1934), associated with the mouse as a vector; the virus of pseudo-lymphocytic meningitis found in two cases only, both in England, by MacCallum, Findlay and Scott (1939); and the virus associated with swineherd's disease—la maladie des porchers—a condition occurring in contiguous parts of France, Italy and Switzerland.

The symptomatology is fairly uniform for all types, but in lymphocytic choriomeningitis there is often a precursory illness of an influenza-like nature lasting one to three weeks with fever, headache, generalized pains and symptoms of an upper respiratory infection (Baird and Rivers, 1938). Symptoms of the meningeal phase are fever 100 to 103° F., a convulsion in children, headache, backache, nausea, vomiting, an irritable wakefulness or drowsiness or delirium, Kernig's sign and in some cases papillœdema, seventh nerve palsy, extensor plantars. The meningeal condition lasts on an average seven to ten days, ending in recovery. Neurological sequelæ are rare, but Barker and Ford mention a case which developed a spastic paralysis of the legs due to a spinal arachnoiditis. The cerebro-spinal fluid is clear or cloudy, cells 50 to 3,000 per c.mm. chiefly lymphocytes, sometimes neutrophils predominate at first, usually no fibrin clot on standing, protein 50 to 200 mgm. per 100 c.cm. Chlorides and glucose are normal, though in first few days slight decreases may occur, cultures negative.

Up to 1942 the figures for choriomeningitis in America were thirty-six proved cases, of which three presented in addition encephalomyelitic signs, and five in this country. The virus is supposedly spread by mouse-contamination and not by droplet infection from man to man, but has also been isolated from the spleen in dogs. In the human infection it can be recovered from the blood early in the illness and from the cerebro-spinal fluid in the first seven to ten days. A leucopenia is commoner than a leucocytosis in the blood. That this condition occurs in a subclinical form is suggested by the fact that in the sera in 10 per cent. of a thousand individuals chosen at random without any history of nervous disease, neutralizing bodies to the virus were obtained.

The pathology consists of a moderate small-celled infiltration of the meninges, ependyma and choroid plexuses, and to a less degree of the perivascular spaces.

In contradistinction to tuberculous meningitis the onset is usually acute, the preceding health good except for a mild catarrhal complaint perhaps, a restless wakefulness commoner than lethargy, a high rather than low lymphocytosis in the cerebro-spinal fluid, and the chlorides and sugar if disturbed soon return to normal figures in place of becoming steadily diminished.

Treatment.—There is no specific treatment as the virus occurs intracellularly beyond the reach of circulating antibody introduced artificially.

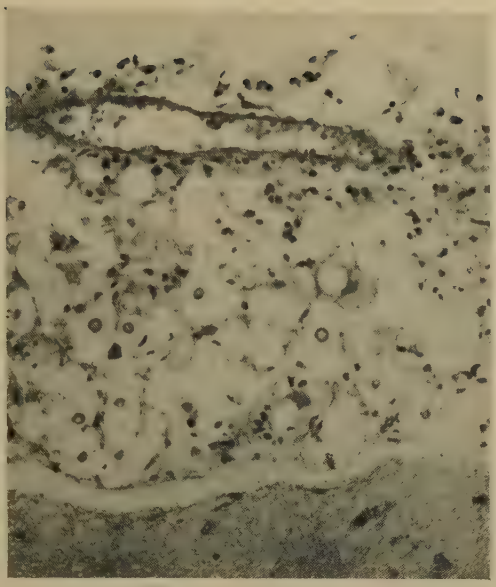

FIG. 353.—TORULA IN LEPTOMENINGES OF TEMPORAL LOBE BELOW A VESSEL AND SOME SLIGHT CHRONIC INFLAMMATORY INFILTRATION.

(By courtesy of Prof. Dorothy Russell.)

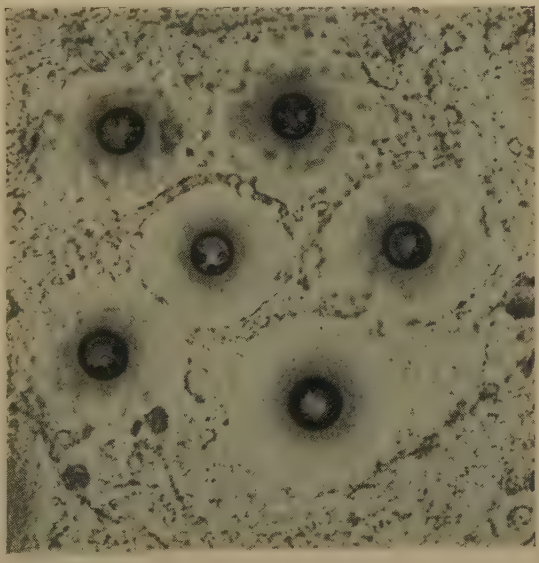

FIG. 354.—TORULA IN BASAL GANGLIA; SIX ORGANISMS WITH THEIR CAPSULES.

(Magnification *circa* × 1,000.)

(By courtesy of Prof. Dorothy Russell.)

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Torula meningitis, due to a yeast-like organism, *Torula histolytica*, or *Cryptococcus meningitidis*, was first described in 1861, and up to 1941 some seventy-nine cases were reported, mostly in adults. Reeves, Butt and Hammack described a case in a girl of fifteen, and Marshall and Teed another in a girl of nine years. The infection can involve several organs, and probably enters by the respiratory system or possibly the intestinal tract. With a meningeal invasion the torula gives rise to pial congestion, small hæmorrhages and a granulomatous exudate at the base of the brain.

The symptoms may be acute, but most often are insidious in onset and resemble those of tuberculous meningitis, cerebral abscess or tumour. Fever is slight, headache, nausea, vomiting, stiff neck are present, and papillœdema giving place to atrophy has occurred. The course may be prolonged and is usually fatal. The cerebro-spinal fluid pressure is high, 250 to 300 mm., and yeast cells are obtained in direct smears, or by culturing the centrifugalized deposit. A moderate lymphocytic pleocytosis is present and some increase of protein. Most cases have been diagnosed on histological examination of the brain. Some claims have been made that sulphonamide therapy inhibits the growth of the organism.

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INTRACRANIAL ABSCESS

Introduction and ætiology.—Abscess of the brain is not a common condition in children, and is most often a complication of otitis media, much less frequently of cranial trauma. In cases of otitic origin, infection may be by local spread from a thrombosed and septic lateral sinus along penetrating blood vessels, or occur via the blood stream and the abscess may not be on the side of the affected ear. In early infancy, cerebral abscess, commonly about the age of three months, is usually due to infection most often staphylococcal of the ear, skin, or to facial sepsis. In rare cases no extracranial infective focus has been found. The heart tends to enlarge (Farley), and an increase of cells, chiefly polymorphonuclears, is found in the cerebro-spinal fluid. Abscesses of otitic origin develop usually in the tempero-sphenoidal lobe, less often in the cerebellum. The cerebral tissues present first a stage of encephalitis, followed by one of pus formation, which may become encapsulated.

Symptomatology.—There is usually a history of chronic ear disease

and often an arrest of aural discharge. Sometimes after a mastoidectomy a persistence of an elevated and irregular temperature, an accelerated pulse, may indicate the need of exploring the lateral sinus, when, if symptoms continue, abscess formation may be suspected.

Early symptoms of intracranial abscess are fever, malaise, anorexia, and a rapid pulse. Vomiting and shivering may also be noted. In a case of temporal lobe abscess, tenderness may be elicited by percussion over the temporal bone. Interference with the pyramidal system is first indicated by slight weakness of the opposite side of the face on showing the teeth. Further signs are diminished abdominal reflexes and an equivocal plantar response on the contralateral side of the body. Disturbance of the fibres of the optic radiation in the temporal lobe gives rise to homonymous hemianopia. At first there is usually an upper quadrantic hemianopia of the opposite fields of vision, as the abscess tends to commence its development in the lower part of the temporal lobe. Aphasia in the naming of objects occurs when the abscess is left-sided in a right-handed subject. Convulsions may also occur.

With an abscess in the posterior fossa, suboccipital headache, dizziness and vomiting on sudden movements, are observed. A cerebellar abscess is usually laterally placed, and gives rise to nystagmus, and unilateral signs, mis-pointing in the finger-nose test, on the same side as the abscess. The child lies curled up in bed, usually on the side of the abscess, and resents being moved.

A low grade of papillœdema is observed in many cases, but tends to develop more quickly and to a greater extent when the abscess is in the posterior fossa. At a more advanced stage of intracranial abscess generalized headache, slowing of the pulse, more frequent vomiting and drowsiness are present.

There is some evidence that a localized encephalitis of the temporal lobe due to otitic infection may develop without abscess formation. The clinical signs are the same as those already described. Adson records three instances of this nature in cases of chronic middle ear disease, where at operation in search of an abscess no pus could be discovered. Recovery took place.

The cerebro-spinal fluid in cerebral abscess is clear and colourless, pressure moderately raised, protein content increased, and usually a moderate pleocytosis of ten to a hundred cells, polymorphs and lymphocytes. The chloride and sugar contents are normal.

Treatment.—From the moment that a brain abscess has been suspected every attempt should be made to maintain the general state of the patient; the longer active surgical treatment can be delayed, within reason, the better the eventual outlook. The successful treatment of this condition depends upon allowing sufficient time to elapse for the abscess to become firmly encapsulated, for attempts at drainage in the first few days lead only too often to disaster.

The advent of the sulphonamide group of drugs and of penicillin have unquestionably improved the prognosis in intracranial suppuration, the risks of early meningitis and extension of the abscess with rupture into

the adjacent ventricles being diminished. In occasional cases spontaneous resolution appears to take place without involving surgical aid.

A nine-year-old girl had been submitted eleven days before admission to mastoidectomy following acute otitis media; six days later she became drowsy and the following day showed neck rigidity, positive Kernig and a raised cerebro-spinal fluid pressure with fluid containing 8 lymphocytes per c.mm. and 50 mgm. of protein.

When admitted to the neurosurgical department she was drowsy, ill, showed bilateral early papillœdema, right sixth nerve palsy and slight left-sided pyramidal signs. Immediate penicillin and sulphonamide therapy was commenced and four days later a ventriculogram revealed considerable shift of the whole system to the left side (fig. 355) but exploratory needling of the right hemisphere encountered no abscess. Three weeks later her condition was greatly improved and a second ventriculogram showed a normal system

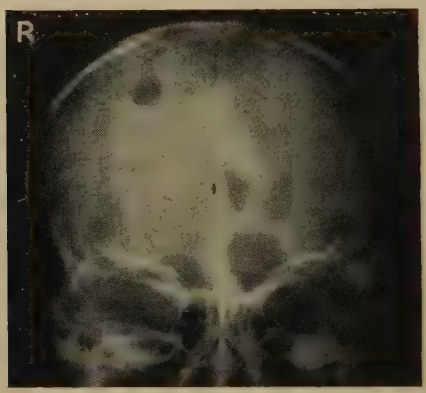

FIG. 355.—ANTERO-POSTERIOR VENTRICULOGRAM.

Showing marked shift to the left side, indicating early stage of abscess formation.

FIG. 356.—ANTERO-POSTERIOR VENTRICULOGRAM.

Taken three weeks later after a course of penicillin and sulphonamide, showing return of ventricular system to normal position as a result of resolution of the infective process.

(fig. 356). At the time of discharge from the department she was perfectly well and exhibited no abnormal signs in the central nervous system except a subsiding papillœdema.

Here is a case where a space-occupying lesion was shown by ventriculography and subsequently disappeared, presumably indicating resolution of a diffuse inflammatory encephalitis which would otherwise have progressed to abscess formation.

When abscess formation has been established surgical treatment becomes inevitable and is designed to reduce intracranial tension and prolong the life of the abscess to a point where it is completely and firmly encapsulated.

There is now good reason to believe that the capsule of an abscess develops most rapidly on its cortical aspect and only slowly on its deep or ventricular aspect. Usually the first step in surgical relief is designed to relieve tension within the abscess cavity by tapping and thus to avoid

the ever present danger of rupture through the weakest part of the wall into the ventricular system.

Tapping is undertaken usually under local anæsthesia through a 3 cm. incision over what is believed on clinical grounds to be the most superficial part of the abscess. A 1 cm. burrhole is made in the bone and then through a 3 mm. nick in the dura the brain needle is inserted into the abscess cavity. Pus is withdrawn by aspiration and, when 20 to 30 c.cm. have been removed, a few c.cm. of thorotrast are injected to render the abscess radio-opaque. It is wise not to remove too much pus at the first tap or great reduction in tension may allow the brain to fall away from the dura and permit infection of the adjacent sub-arachnoid space. Quite a small amount of pus aspirated will help to tide the child over the next few days and, during this period, X-ray pictures should be taken accurately to localize the now visible lesion. At the end of the aspiration the wound should be completely closed in three layers with interrupted silk sutures.

One or more further taps may be required before more extensive treatment is adopted depending upon the rapidity with which the abscess refills and upon the general condition of the child. Subsequent taps may be made, without anæsthesia, by passing a brain needle through the original incision or through a more suitably placed incision whose site is indicated by the radiographic localization.

If the bacteriology of the pus from the first aspiration has shown penicillin sensitive organisms, subsequent aspiration of the abscess may be combined with injection of penicillin (mixed with thorotrast) into the cavity, thus making a direct assault upon the organisms to aid that supplied by the oral administration of sulphamezathine and intramuscular injection of penicillin.

Occasional patients will recover with aspiration alone as shown by the following case record :

A sixteen-year-old girl was admitted comatose with bilateral papillœdema, nystagmus, left facial weakness and left-sided cerebellar signs in the limbs. Six weeks previously she had had an influenzal attack with earache. Three to four weeks later the left ear became painful and a purulent discharge was noticed. A mastoidectomy was performed and granulations found covering the dura mater of the posterior fossa. Her condition continued to deteriorate in spite of a course of sulphadiazine (18½ grammes) and the day before admission a lumbar puncture was performed : the pressure was 240 mm. of cerebro-spinal fluid, but the fluid itself was normal. She was operated upon two days after admission, a single burrhole being made over the left cerebellar hemisphere. The abscess, thinly encapsulated, was entered at a depth of 3 cm. and 8 c.cm. of pus obtained. 1 c.cm. of thorotrast and 10,000 units of penicillin were injected. Immediate improvement resulted but a second tapping of the abscess was required about ten days afterwards. From then onwards the patient returned to normal health, the mastoid wound healed and all abnormal signs in the central nervous system disappeared.

X-ray pictures show the thorotrast presumably embedded in a small mass of fibrous scar, but no remaining abscess cavity. Six months later she was perfectly well and back at her work as a nursery maid.

More usually, however, further surgical intervention is required of which two methods may be mentioned in more detail.

With a well-encapsulated abscess, several weeks or even months after the primary treatment was commenced, total extirpation gives good results. The procedure is to turn down an osteoplastic flap, as for removal of a tumour, incise the cortex over the most superficial portion of the abscess and then dissect out the thick walled abscess intact. This is a relatively bloodless process and quite simple in a unilocular abscess. In large or multilocular abscesses, however, difficulty will be encountered and the abscess may rupture with soiling of the wound. This is not necessarily disastrous as the abscess may well by now be sterile, or penicillin and sulphonamide treatment suffice to prevent infection.

If radical excision be considered unsuitable the next stage is to coax the abscess cavity, in the walls of which the radio-opaque thorotrast

FIG. 357.—SEMI-AXIAL ANTERO-POSTERIOR VIEW OF SKULL.

Showing abscess in left cerebellar hemisphere filled with thorotrast.

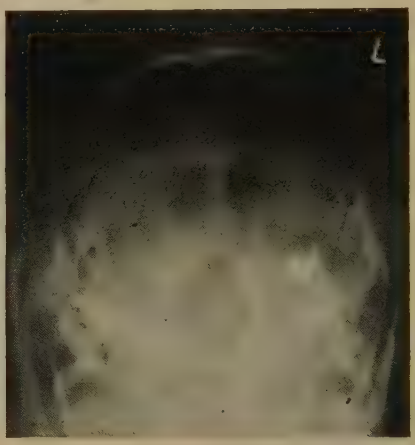

FIG. 358.—SIMILAR VIEW OF SAME PATIENT EIGHT WEEKS LATER.

The abscess has shrunk to a small mass of fibrous tissue with no remaining abscess cavity as a result of repeated aspiration alone.

becomes fixed in a week or so, towards the surface of the brain. This is usually achieved by enlarging the scalp incision in cruciform manner or by making a small flap and removing a circle of bone some five to six cm. in diameter. The dura is left closed but the wound is lined with a sheet of gutta percha and plugged to keep it open.

Some days, or a week, later the dura may be opened in radial fashion and the wound again plugged, herniation of the brain now being controlled by repeating lumbar puncture. After the lapse of a few days the brain will have become adherent to the overlying membranes at the margins of the bony opening and the abscess should have travelled nearer to the bony opening in response to herniation of the brain and local reduction of pressure.

Finally the superficial brain tissue is sucked away and the abscess capsule exposed. The abscess wall is incised in cruciform manner, the

escaping pus sucked away and the edges of the capsule sutured to the surrounding galea to maintain it in position. This stage of the treatment is completed by plugging the now empty abscess capsule with ribbon gauze to prevent loculation by collapse of the wall. Dressings are done every few days and on each occasion some of the gauze pack will have been extruded, and may be cut away, as the abscess evaginates itself. In the end the abscess is wholly everted so that the pack is expelled and the surface of the wound consists of the inner aspect of the abscess wall. The scalp flaps may now be allowed to fall over this granulating surface which soon heals.

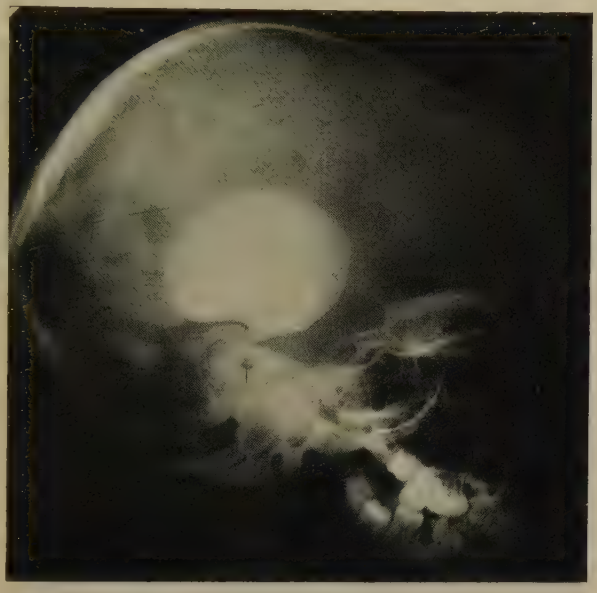

FIG. 359.—LATERAL VIEW OF SKULL.

Showing large temporal abscess filled with thorotrast after puncture and aspiration through a single burrhole.

Quite a number of minor operations may thus be required to deal with any given abscess and between any two stages further tapping of the cavity may be required, especially if the deep surface of the abscess encapsulates slowly, to delay the procedure for safety's sake. Repeated X-ray examinations will give precise information of the behaviour of the abscess wall by reason of the thorotrast therein and will generally be required at weekly intervals. In all some six to twelve weeks are required to treat intracranial abscess by this method of *marsupialization*, but the results are undoubtedly good (fig. 359 to 364).

Radical excision is probably the more perfect method in that scarring is reduced to a minimum, whilst marsupialization leaves a scar in the brain adherent to the scalp which may later be the cause of traumatic epilepsy.

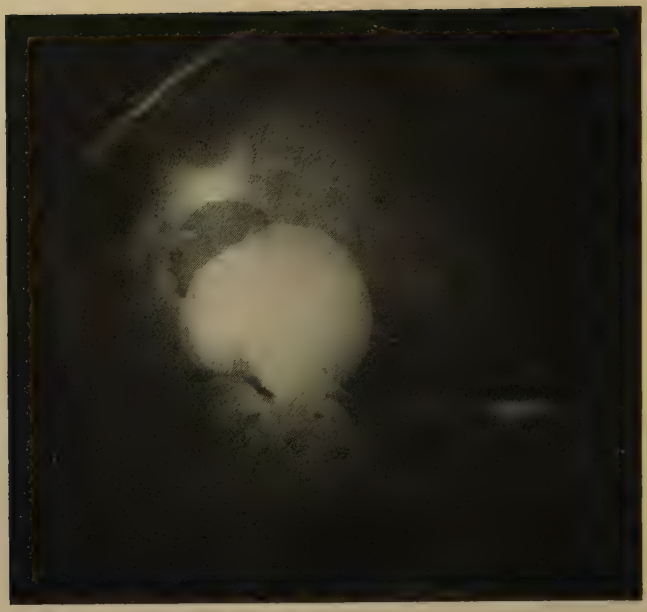

FIG. 360.—SIMILAR VIEW THREE DAYS LATER.

Showing enlargement of the bone defect and thorotrast being fixed in the developing abscess capsule.

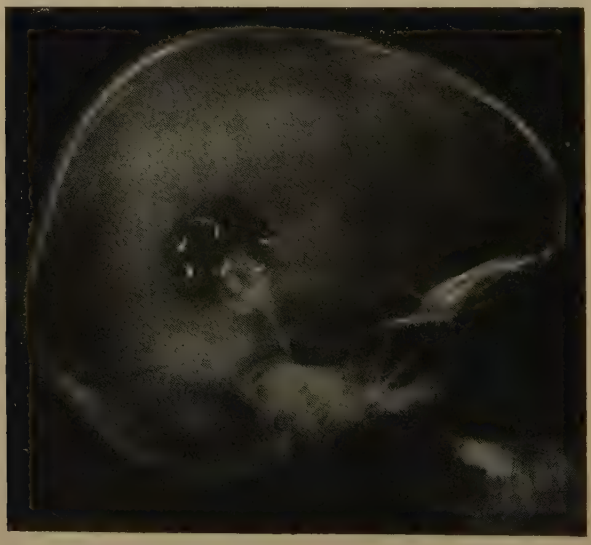

FIG. 361.—SIMILAR VIEW NINE WEEKS LATER AFTER MARSUPIALIZATION.

Showing great shrinkage in size of abscess. The direction of travel of the abscess is shown by the drawn out scar extending from infected petrous bone, made visible by contained thorotrast.

FIG. 362.—EARLY STAGE OF MARSUPIALIZATION.

Triangular scalp flap turned back, dura bulged forwards by abscess lying deep to it.

FIG. 363.—LATER STAGE, SHOWING ABSCESS CAVITY REDUCED TO A SMALL SLIT.

The majority of the capsule is completely everted and raised above the surrounding scalp.

FIG. 364.—FINAL STAGE IN MARSUPIALIZATION.

The scalp flap has been allowed to fall back and the wound is granulating well.

In isolated cases, particularly where the causal infection arises from the posterior ethmoidal air cells or from the deeper parts of the petrous temporal, the abscess travels reluctantly, if at all, towards the bony decompression and, once a good capsule has been developed, it may then be safer to drain the abscess through the region from which infection originally reached the brain. In the main, however, brain abscesses should not be drained through the infected bony cavities from which they originated such as the frontal sinus, ethmoidal air cells, or petrous bones. It is bad policy to enter the cranial cavity through a septic channel unless absolutely forced to do so (fig. 365 to 369).

The primary cause of the abscess whether it be from the ear or nose has also to be considered, but radical cure should not be attempted until the abscess is under control, if not cured. When the general condition of the child permits and the abscess is encapsulating well it may be wise to have the mastoid, frontal sinus or other primary focus dealt with by an otorhinolanrygologist, but in most cases this may wait until the abscess has healed.

Many methods have been devised for the treatment of brain abscess and no attempt has been made to survey them here. Each neurosurgeon tends to a slightly different line of approach which no doubt indicates that perfection is as yet far from attainment.

It is safe to say that surgical success in the treatment of brain abscess depends largely upon the experience of the surgeon ; the longer his surgical life extends the greater is likely to be his rate of cure.

Results of treatment.

In a series of seventeen cases of intracranial abscess in children treated during a period of four years, twelve recovered and five died. Of the

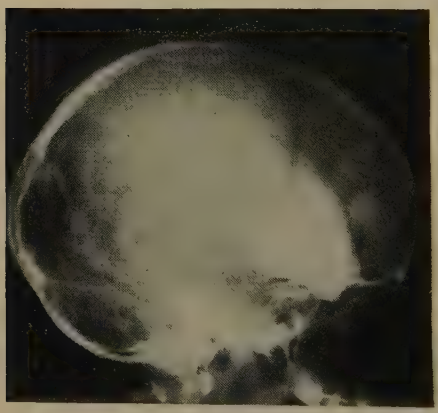

Fig. 365.—Lateral X-ray Picture showing Presence of large Pear-shaped Abscess originating from Infection of Ethmoid Air Cells.

It has been tapped and a frontal bone defect has been made to coax the abscess away from its point of origin.

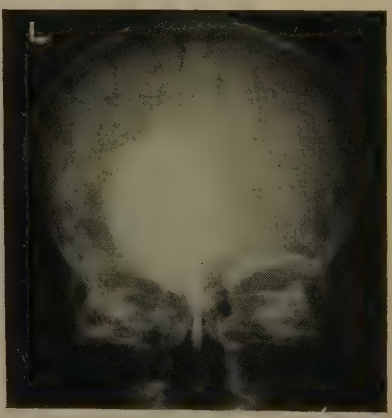

Fig. 366.—Antero-posterior View of same Patient.

Showing point of origin from ethmoid air cells.

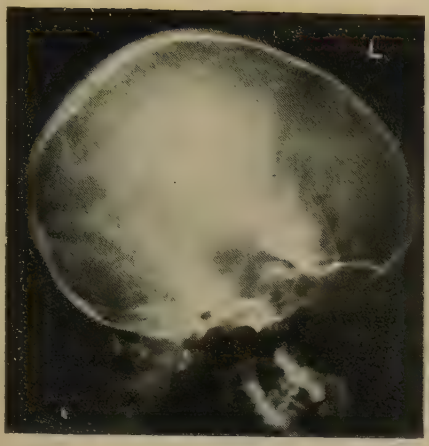

FIG. 367.—LATERAL X-RAY PICTURE, AFTER REPEATED TAPPING OF ABSCESS.

Showing failure of abscess to travel forwards to site of decompression.

FIG. 368.—LATERAL X-RAY PICTURE, AFTER DRAINAGE OF ABSCESS THROUGH ETHMOID REGION.

Showing marked shrinkage in size and thickening of wall.

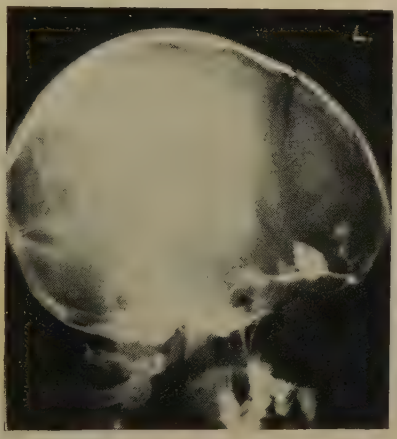

FIG. 369.—SHOWING COMPLETE DISAPPEARANCE OF ABSCESS CAVITY.

There remains only a wall of thorotrast containing scar tissue. The remnants of a second abscess, which developed in the needle track used for tapping the original abscess, can also be seen.

deaths three occurred before the advent of penicillin, one being a child with a fulminating infection producing extradural, subdural and intracerebral collections of pus, with spreading meningitis from an acute osteomyelitis of the frontal bone. The other two were patients with multilocular frontal abscesses. The remaining two children died from rupture of an acute abscess into the ventricular system soon after admission. It is likely that some at least of the first three deaths could have been averted had penicillin then been available.

TABLE 50

Site of Abscess	Number of Cases	Origin	Treatment	Died	Recovered
Frontal . .	7	4 frontal sinus 1 traumatic 1 ethmoid cells 1 blood borne	6 marsupialized 1 marsupialized and also drained through ethmoids	4	3
Temporal	5	5 otogenic	4 marsupialized 1 tapped	1	4
Cerebellar .	5	5 otogenic	3 marsupialized 2 tapped	0	5
	17			5	12

The results of treatment, with a recovery rate of 70 per cent., are encouraging and now, with the additional aid of penicillin, a still higher rate of recovery may be hoped for.

It should be emphasized that the treatment is prolonged, requires unremitting care and attention to detail and must be carried out by the surgeon himself in a department of neurosurgery. An attempt to delegate stages of treatment to assistants, even the frequently required dressings, is likely to lead to disaster.

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ACUTE HEAD INJURIES

From early infancy and throughout childhood most head injuries are sustained from a fall. The common manner of injury is by a violent movement of the head against a solid substance, rather than by the sudden impact of a missile against the stationary head. From an initial inertia the brain is jerked into a secondary momentum with a final sudden arrest as the skull comes in contact with a hard surface. Denny-Brown and Ritchie Russell's studies attest that concussion is more easily produced by the *acceleration* method than by compression when the head is stationary and a striking force comes against it. They hold the theory of concussion as the direct effect of physical stress or mechanical jarring upon neurons and not as a vascular phenomenon. Experimentally, acceleration concussion was not found to be associated with any significant change of intracranial pressure. Displacement of the brain and the shock of sudden downward expression of cerebro-spinal fluid into the posterior fossa have an immediate widespread paralytic effect upon cerebral neurons including those of the brain-stem, as shown by a short period of unconsciousness or concussion and alterations of the respiratory and pulse rates, of blood pressure and of the corneal reflex. Jefferson suggests that traumatic stupor or prolonged unconsciousness

and pupillary changes depend upon a greater degree of downward disturbance towards the posterior fossa affecting sleep-controlling centres in the upper pons, hypothalamus, anterior periventricular grey matter of the third ventricle, and oculo-pupillary centres around the aqueduct and in the quadrigeminal plate. The petechiæ of contusion and the grosser lacerations when in non-silent areas produce focal signs, and œdema is one of the possible causes of delayed stupor.

Clinically, the symptoms of intracranial trauma may either be immediate in onset or delayed. Most cases are of the "closed" type,

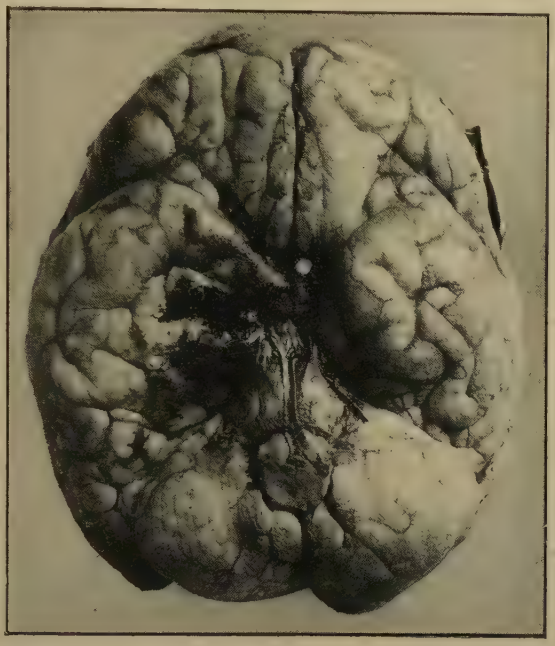

FIG. 370.—LATE APOPLEXY: BRAIN OF A CHILD AGED TWELVE, SHOWING AN AREA OF SOFTENING ON THE INNER SIDE OF THE RIGHT TEMPORO-SPHENOIDAL LOBE, HÆMORRHAGE FROM WHICH CAUSED DEATH OF THE CHILD SIX WEEKS AFTER THE ORIGINAL INJURY.

(From photograph kindly lent by Dr. A. H. Miller.)

that is, the skulls are intact radiographically or show fissure fractures only. In thirty-five "closed" cases Northfield found cephalhæmatoma in ten, fracture of the vault in fifteen, and concussion in fourteen. Concussion occurs less often than in adults with closed injury because of the greater elasticity of the child's skull, but fissure fractures are commoner.

The other symptoms can to some extent be related to the different types of vascular lesion, subarachnoid hæmorrhage, contusion or cerebral grazing, cerebral œdema, subdural, extradural hæmorrhages and sepsis. Each has distinguishing features, but in practice the picture is often blurred or composite.

(1) Subarachnoid hæmorrhage.—Concussion is not always present. The onset of headache, drowsiness, stiffness of the neck, pyrexia, unconsciousness, may not occur until after one or two hours. Slight paresis is common on the same side of the body as that of the head struck, as the vessels are usually damaged by contre-coup. The cerebro-spinal fluid is deeply bloodstained.

(2) Contusion.—The lesion is a localized meningo-cortical hæmorrhage. When in a non-silent area of the brain the onset of local paralysis is rapid, but seldom a complete hemiplegia. Jacksonian fits, indicative of the site of the lesion, often develop early in the first one or two days. In severer grades of contusion some xanthochromia of the cerebro-spinal fluid will be present after a few days.

(3) Extradural hæmorrhage is uncommon and by itself likely to give rise to a gradual, rather than a sudden, oncome of hemiplegia over several days, with possibly Jacksonian epilepsy of later onset. The patient regains consciousness only to relapse some hours later into unconsciousness. The temperature and pulse-rate are raised; delirium may pass into stupor. The cerebro-spinal fluid is normal, under pressure, contains a few cells, or may be slightly yellow.

(4) Subdural hæmatoma in infancy appears to be commoner than was previously believed, probably because it is more commonly thought of and the diagnostic procedures necessary more often carried out. Trauma at birth or subsequently is the outstanding cause and as regards post-natal trauma it is not necessarily severe. Infection, vitamin C deficiency and malnutrition are also blamed. The majority of cases occur in the first six months of life. Bilateral effusion of blood between the dura and pia-arachnoid is more common than unilateral effusion. Clotting takes place and this is followed by the development of a tough capsule. Early symptoms are vomiting, irritability, lethargy, failure to gain weight and reluctance to feed. Later convulsions occur, generalized or localized, the temperature rises and the head enlarges with bulging of the fontanelle. Reflexes are exaggerated and retinal hæmorrhages are commonly found. Diagnosis is established by tapping the suspected area with a lumbar puncture needle inserted under local anæsthesia in the frontal suture line. Fluid obtained may be blood-stained and on standing the supernatant fluid is xanthochromic.

(5) Œdema of the brain is a common complication of all forms of cerebral injury, either locally around a traumatic lesion, or at the various poles, but seldom generalized. A delayed onset up to about the fourth day of stupor, irritability, paralysis without definite focal signs is more often due to cerebral œdema than to secondary hæmorrhage.

(6) Sepsis.—A fracture of the skull not always visible by radiography communicates with one of the facial sinuses; signs of meningitis, vomiting, headaches, pain in the neck develop; the fluid contains a high polymorph count.

Sequelæ of head injuries in children after birth.—The child tolerates a head injury better than an adult, recovers more rapidly and completely, and more often escapes late effects. Headache is not a

common post-concussional state in the child. Only after severe injury does mental alteration occur. Residual paralyses and epilepsy are uncommon except after penetrating wounds of the skull. Fracture through the base of the skull causing damage to the infundibular region presumably by extravasation of blood has been known to give rise to obesity with bulimia, or to diabetes insipidus.

Treatment.—Injuries of the scalp and bone are necessarily important complications of head injuries, requiring thorough examination and cleansing, but there is no urgency about their surgical treatment. It is more important to combat shock by getting the child warm in bed, giving fluids by mouth or intravenously, and sulphonamide or penicillin in cases with scalp wounds and fracture. At a first examination any abnormal neurological signs, the temperature, pulse and respiratory rates, and if possible the blood pressure are recorded. A later slowing of the respiratory and pulse rates and a rising blood pressure indicate the presence of a progressive lesion. After twelve to twenty-four hours' rest, if possible, radiological examination includes a straight postero-anterior, a semi-axial sagittal antero-posterior to show up the whole of the occipital bone, and a stereoscopic lateral view.

Next, lumbar puncture is performed and the presence or absence of blood noted. The pressure may be low initially when only a small amount of fluid should be withdrawn, or raised and a considerable quantity of fluid can safely be taken off. Low manometric readings are as common as high ones, but usually they lie within normal limits. High pressures after head injury may reach a level of about 200 mm. water, rarely 300 mm., and are not comparable to the high levels reached in cases of cerebral tumour and meningitis. Ritchie Russell found no evidence that increased intracranial pressure by itself caused death in head injury. In cases with raised pressure, to reduce headache and as it does not promote renewed bleeding McKissock and Brownscombe (1941) advocate lumbar puncture, and dehydration therapy using a limited fluid intake of 30 oz. per diem, or rectal injection of one or more ounces of 50 per cent. magnesium sulphate, or 25 to 50 c.cm. of a 5 per cent. sucrose solution intravenously. Severe restlessness is treated by injection of soluble phenobarbitone, $\frac{1}{2}$ to 1 grain. In mild cases a child need only be kept in bed for a few days, and even with a fracture, provided no signs of continued cerebral dysfunction exist, a child may be up and about in seven to ten days.

When prolonged or delayed stupor with signs of a progressive lesion exist subdural and extradural bleeding must be searched for. Plain X-ray pictures will not help, and encephalography or ventriculography are more exacting to the patient's strength, though often useful at later stages, than tapping by needle under local anæsthesia. Subdural hæmorrhage as already described can be unilateral or bilateral. From examination of ninety-eight cases in children, Ingraham and Matson describe the membrane-contained clot to extend from the parietal area well forwards frontally and from the superior longitudinal sinus downwards into the anterior and middle fossæ. If the diagnostic tap shows the presence of

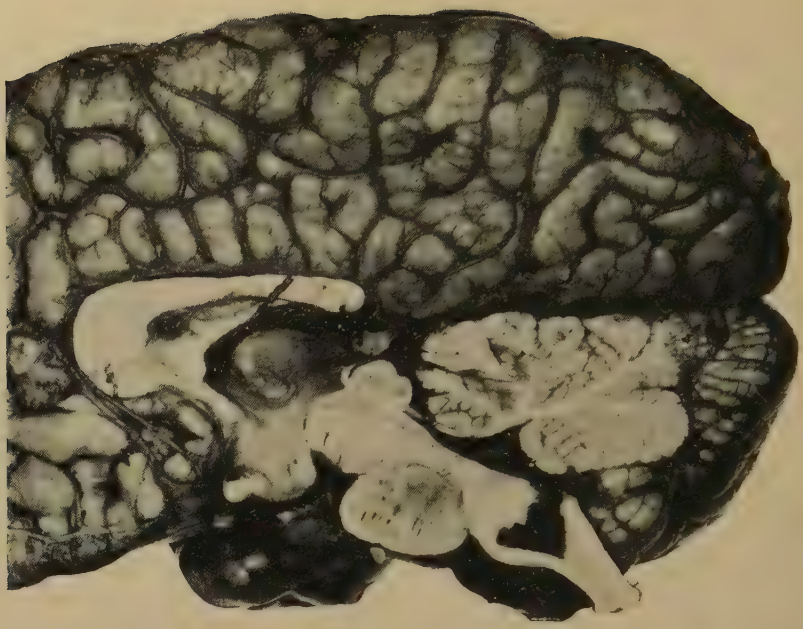

FIG. 371.—HÆMORRHAGE INTO THE MEDULLA AND FOURTH VENTRICLE CAUSED BY A FALL.

The case presented symptoms suggesting a meningococcal meningitis. On lumbar puncture only blood-stained fluid was obtained, and this was thought to be due to puncture of a vessel. Note the hæmorrhage in the ventricle and in the substance of the medulla.

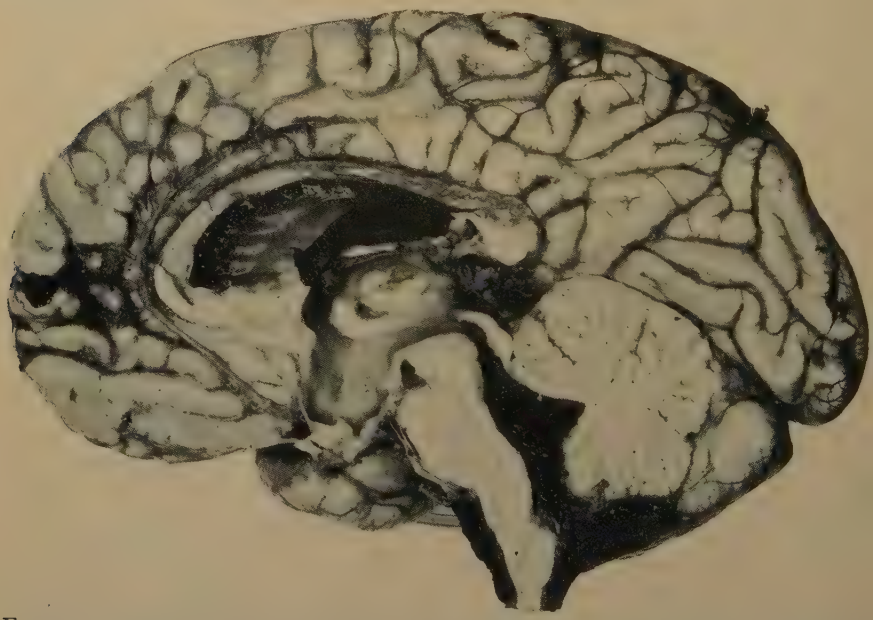

FIG. 372.—HÆMORRHAGE INTO LATERAL, THIRD, AND FOURTH VENTRICLES, AND ALONG THE VENTRAL SURFACE OF THE CORD, CAUSED BY PUNCTURE OF THE LATERAL VENTRICLE UNDERTAKEN FOR THE RELIEF OF PRESSURE.

blood stained fluid a burr-hole exploration is carried out to reduce tension, and finally at a later date a bone flap is turned down and the clot removed. In long standing cases the lining membrane especially on the outer aspect of the clot progressively thickens.

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INTRACRANIAL HÆMORRHAGE

Intracranial hæmorrhage, exclusive of the important group of cases which occurs at birth, is rare in childhood. Out of 10,150 consecutive post-mortem examination in children under twelve years of age at The Hospital for Sick Children, Great Ormond Street, Sheldon found fifty cases of intracranial hæmorrhage, which is rather less than a half per cent. of the total figure. The number of cases falling in the first year of life was considerably greater than in any subsequent year.

Newborn.—Intracranial hæmorrhage, asphyxia, prematurity, malformations and infection are the major causes of stillbirth and neonatal death. Browne in 200 deaths (120 stillbirths, 80 neonatal) found intracranial hæmorrhage in 59, or 29·5 per cent., 35 among the neonates and 24 among the stillborn. In the 120 stillbirths, asphyxia accounted for 49, or 40 per cent. Of the 200, 95 were prematures of which 39 were stillborn (asphyxia 11; cerebral hæmorrhage 5) and 56 neonatal (asphyxia 1; hæmorrhage 22). Hæmorrhage is more common in the neonates than in the stillborn. MacGuiness in 316 fœtal and infant deaths found cause of death in the 184 mature to be intracranial hæmorrhage 52, asphyxia 23; and in the premature, immaturity was the chief cause in 53, atelectasis 26, and hæmorrhage 26. In neonates with severe lesions such as gross hæmorrhage and septal tears, the average day of death is the third.

The frequency of tears of the tentorium or other dural septa with gross bleeding was 35 (37 per cent.) in 94 autopsies (Browne); 131 (16·4 per cent.) in 800 autopsies (Cruickshank). MacGuiness found the tentorium torn in 92·5 per cent. of cases with septal traumatism, and the falx in three instances only.

The types of birth most often giving rise to intracranial hæmorrhage are difficult and prolonged labour, excessive head-moulding, breech-birth, and precipitate birth. Potter and Adair give the following percentages in various types of delivery: natural cephalic 6·4 per cent.; Cæsarean 10·8; version and extraction 12·5; low forceps 24·5; and mid and high forceps 69·1 per cent.

Symptomatology.—The diffuse nature of the lesions, extracerebral bleeding, intracerebral petechiæ and cellular anoxæmia, and secondary pressure effects upon vital centres in the brain stem tends to cloud any

particular pattern of localized damage. In the severe and obvious cases of birth-trauma two types are roughly outlined.

(*a*) Supratentorial hæmorrhage is indicated by a bulging fontanelle, restless drowsiness, crying, hypersensitivity to stimuli, exaggerated reflexes, twitchings and convulsions. (*b*) Infratentorial bleeding is shown by stupor, uneven respirations, apnœic phases and cyanosis, difficulty in

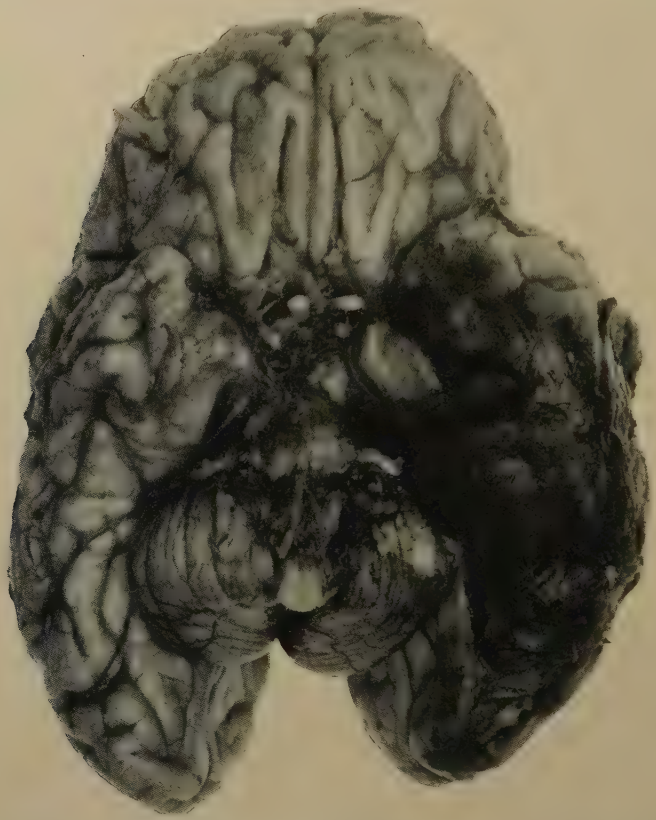

FIG. 373.—BRAIN OF INFANT, SHOWING LARGE HÆMORRHAGE INTO THE SUBSTANCE AND ON THE SURFACE OF THE LEFT TEMPORO-SPHENOIDAL LOBE, DUE TO INJURY BY FORCEPS AT THE TIME OF BIRTH.

sucking, and blood is usually present in the cerebro-spinal fluid. Other signs in either type are oscillatory jerks of the eyes, and hæmorrhage in the anterior ocular chambers and punctate ones on the retina.

The occurrence of sudden attacks of respiratory arrest in infants of a few hours to a few weeks of age has been described by Still and by Kirkwood. Capillary hæmorrhages in the pons and medulla have been found in such a case.

TREATMENT.—Operative measures for the relief of intracranial hæmorrhage at birth have given poor results except in some cases of

subdural hæmorrhage (see p. 1242). The reason is that in addition to the superficial bleeding, the intracerebral damage due to anoxæmia, œdema, petechial bleeding is unalterable. Severe bleeding with septal tears is always fatal.

General measures aim at keeping the infant quiet, warm and disturbed as little as possible. Sedatives and oxygen should be given as required. For the relief of intracranial pressure the rectal introduction of 2 to 3 oz. of a 10 per cent. saline solution (one teaspoonful of salt in two ounces of water) is useful and can be repeated four-hourly according to the symptoms.

Lumbar puncture is of doubtful value, as the advantage aimed at in lowering the intracranial pressure is usually outweighed by the frequency of " dry-puncture " in the newborn, and by the amount of disturbance and exposure entailed in carrying out the procedure. Vitamin K can be given if there are signs of progressive bleeding.

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Thrombosis and embolism of cerebral vessels and sinuses.— Thrombosis of the lateral sinus is associated most often with middle ear and mastoid disease. The internal jugular vein may be palpable and tender. When the cavernous sinus is thrombosed, there is always proptosis, œdema of the eyelids and paralysis of ocular muscles. Thrombosis of the superior longitudinal and other sinuses is sometimes discovered *post mortem* in marantic infants suffering from infective conditions. *Treatment* in the case of lateral and cavernous sinus thrombosis consists in giving adequate doses of sulphonamide, or of penicillin, and surgical clearance of the primary focus of infection.

Embolism, usually of the middle cerebral artery, causing hemiplegia, hemianopia, and in some cases aphasia, is liable to occur in subacute infective endocarditis. Cerebral thrombosis and embolism as a complication of one of the infectious fevers are mentioned in another section (ch. XXV). Spontaneous cases in young children of convulsions, vomiting, fever, and hemiplegia are possibly due to intracerebral vascular lesions probably toxic in origin. An example of this kind, a thrombosis of an anterior cerebral artery, is referred to under epilepsy (p. 1156).

Spontaneous subarachnoid hæmorrhage due to leakage or rupture of a congenital aneurysm is less common in children than in adults, but instances have been reported as early as at seven years. The aneurysms develop from a local defect in the arrangement of the elastic tissue in the arterial walls, and are usually situated in the circle of Willis at the junction of the posterior and middle, or middle and anterior, cerebral

arteries, or arise in an artery intracerebrally at some distance from the circle of Willis, as in Hermann and Macgregor's case in a child of four and a half years. The condition may be both familial and hereditary.

Symptoms of meningeal irritation predominate—headache, vomiting, stiffness of the neck, Kernig's sign, and mental confusion. In some cases the onset is sudden with intense suboccipital pain, followed by unconsciousness –an acute cerebro-vascular catastrophe. In others it is insidious with frontal and occipital headache, pains in the back and limbs,

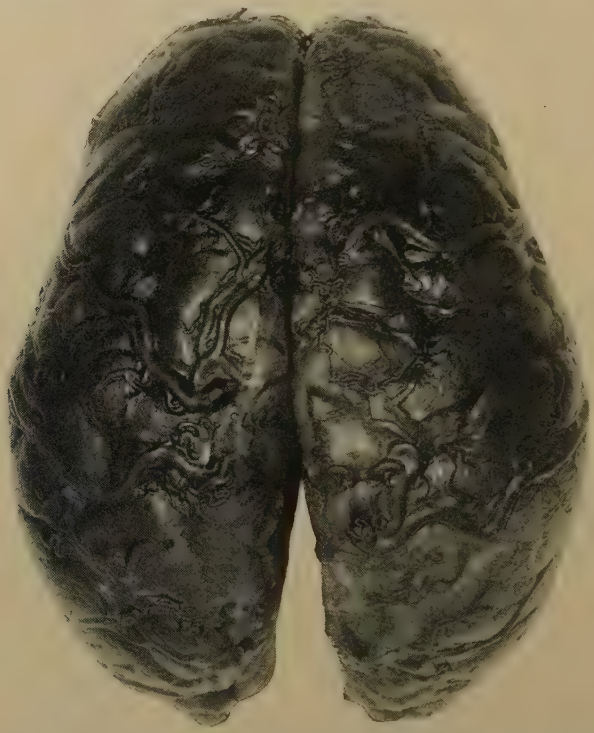

Fig. 374.—Thrombosis of Superior Longitudinal Sinus.

The veins leading into the sinus are thrombosed, and there is extravasation of blood over the surface of the cortex.

vomiting, and a rise of temperature due to hæmolysis of extravasated blood in the subarachnoid space –an aseptic meningitis. The clinical resemblance to "influenza" may lead to an error of diagnosis, or a more sudden attack with recovery may be attributed to "sunstroke."

Albuminuria may be present as in other forms of subarachnoid hæmorrhage (Symonds). With the ophthalmoscope swelling of the discs, retinal and subhyaloid hæmorrhages are observed in some, but not in all cases. Except when the aneurysm is situated and bleeds into the substance of the brain, the cerebro-spinal fluid is heavily blood-stained, and on standing shows a deep yellow discolouration with a sediment of corpuscular debris.

Recovery from an initial aneurysmal leakage often occurs, but when repeated, death is likely to occur at a second to fourth repetition.

The occurrence of hæmorrhage from an intracranial aneurysm has been found in association with coarctation of the aorta. The high blood pressure in the proximal segment of the aorta and its branches may produce the aneurysm by acting upon a congenitally weak spot in the walls of an intracranial vessel (Weber and Bode).

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CEREBRAL DIPLEGIA

Congenital Spastic Paralysis (Atrophic Lobar Sclerosis), Bilateral Hemiplegia, and other types

The title, cerebral diplegia, denoting a bilateral affection of the brain, covers groups of cases of separate ætiology and pathology. Some are due to arrested development or to toxi-infective processes in intra-uterine life—prenatal; others are caused by factors incidental to the processes of birth—natal; and others—post-natal—are of infective origin, sequels of encephalitis or meningitis, or are due to degeneration of neurons from intrinsic causes. These latter are of a progressive nature, and are described later under the title of progressive cerebral sclerosis in young children.

Clinically, it may be impossible to differentiate between a diplegia of antenatal and one of natal origin, but in general certain distinctive features exist. Four types are to be distinguished.

(1) Congenital Spastic Paralysis, and Paraplegia.

(2) Bilateral Hemiplegia, with or without athetosis.

(3) Atonic Diplegia.

(4) Cerebellar Diplegia.

Beside the frequent impossibility of stating whether the paralysis belongs to group 1 or 2, and as the ætiological factors are so numerous, so the anatomical

Fig. 375.—Cerebral Diplegia: Child Attempting to Walk, and showing the Typical Cross-Legged Progression.
(From a photograph supplied by the late Dr. James Collier.)

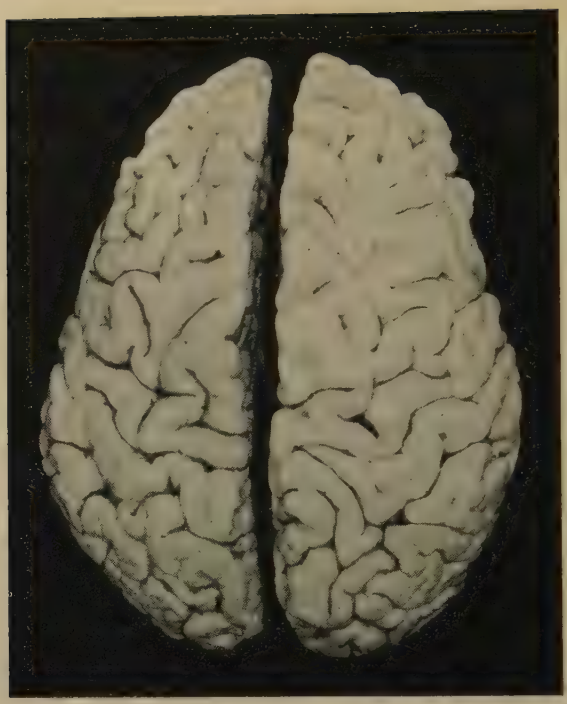

Fig. 376.—Cerebral Diplegia: Brain of a Child with Cerebral Diplegia, showing a General Atrophy of the Cerebral Cortex.
The brain substance was unduly firm and tough.

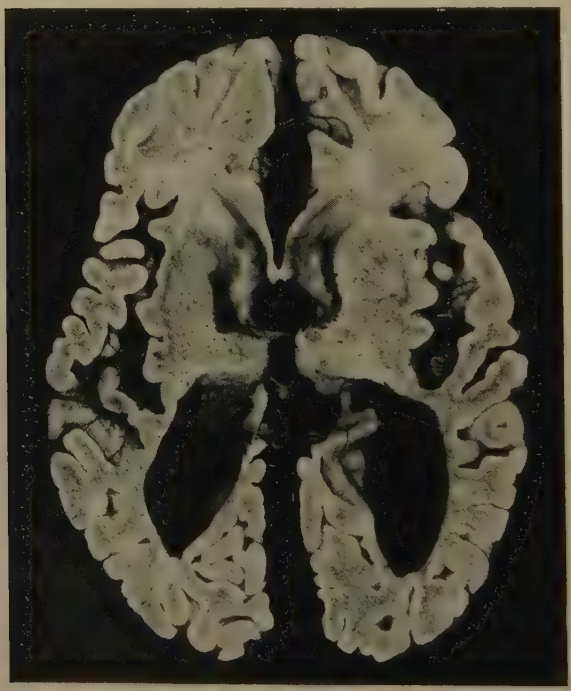

Fig. 377.—Cerebral Diplegia: Horizontal Section of Brain seen in Fig. 376, showing the Atrophy of the Cerebral Cortex and Compensatory Dilatation of the Ventricles.

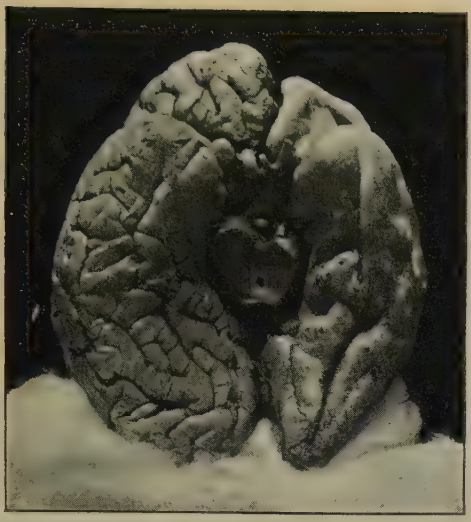

Fig. 378.—Cerebral Diplegia: Brain of an Infant aged Seven Months, showing Arrest of Development of the Left Hemisphere about the Sixth Month of Fœtal Life.

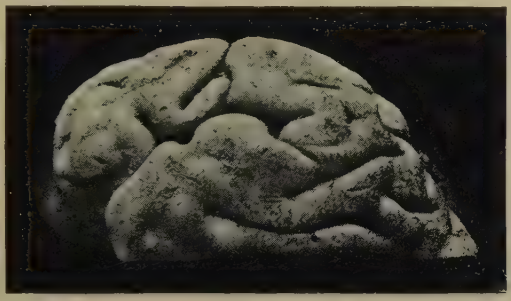

Fig. 379.—Cerebral Diplegia: Lateral View of the Above Hemisphere, showing the Primitive Condition of the Convolutions.

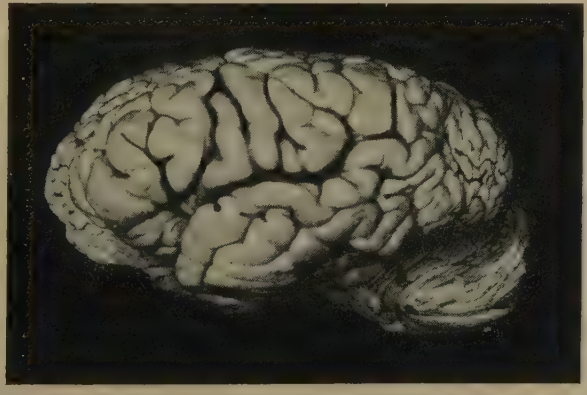

Fig. 380.—Brain of Defective Child, showing Microgyria and an Abnormal Arrangement of the Convolutions.

It will be noted that the microgyria is especially marked in the occipital lobes. In such cases the children are usually blind.

changes in the central nervous system are often variable and non-specific, even in cases of the symmetrical type (Stewart), but the following descriptions are representative of these separate groups.

(1) **Congenital spastic paralysis** is characterized by general rigidity with symmetrical paralysis on the two sides of the body. Rigidity is greater than paralysis, and the muscular power is often surprisingly good. The arms are less affected than the legs. In less severe cases of this type the legs only are paralysed congenital spastic paraplegia. The knees and ankle jerks are exaggerated, but rigidity of the limbs often makes it difficult to elicit them. Ankle clonus is often

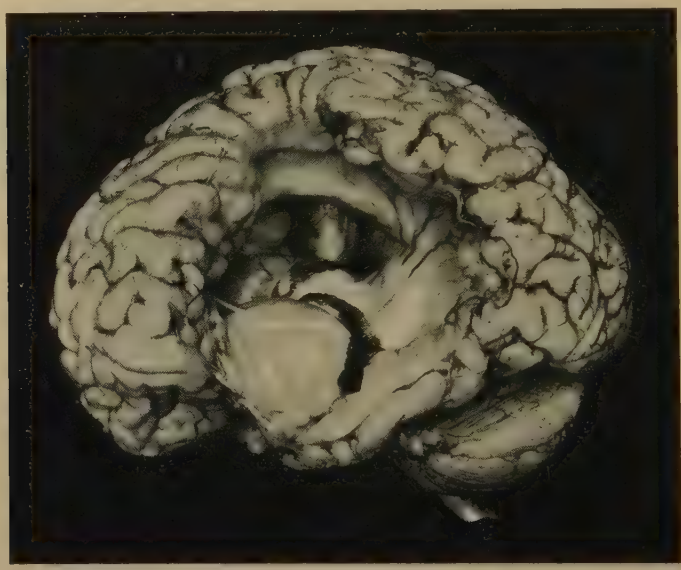

FIG. 381.—CEREBRAL DIPLEGIA: BRAIN OF INFANT, SHOWING ONE FORM OF CEREBRAL DEFECT MET WITH IN THIS CONDITION.

Note the deficiency of the cerebral cortex, and the exposure of the basal ganglia, the lateral ventricles, and the choroid plexuses. The defect was bilateral, though not quite symmetrical.

present, and the plantar responses are extensor. Amentia of greater or less severity is present in all cases. Abnormal movements, athetosis, do not occur in this form of diplegia. A mild degree of congenital spastic paralysis may not attract notice until the child reaches school age, when such signs are observed as awkwardness in the use of the limbs, exaggerated tendon reflexes, some degree of adductor spasm in the thighs, restricted extension of the knee-joint with the thigh flexed, and the plantar will give a doubtful rather than a frankly extensor response.

Post-mortem studies suggest that atrophic sclerosis of the cortex of symmetrical distribution in the two hemispheres is often the anatomical basis of this condition. The *surface* of the brain in the affected areas has a walnut-like appearance from atrophy of the gyri with widening of the

sulci. Symmetrical sclerosis of the upper Rolandic area accounts for paraplegia, of the full extent of the Rolandic areas for diplegia. The degree of amentia present in these cases depends upon the extent to which the sclerosis involves neighbouring areas of the cortex, especially in the prefrontal region. The condition of atrophic cortical sclerosis is antenatal in origin. The symmetry of its distribution makes it unlikely that any crude form of cerebro-vascular lesion, asphyxial or petechial, at birth could be the cause. In a majority of the cases of congenital spastic paralysis the history of the birth is normal. Other appearances seen *post mortem* in cases of diplegia of antenatal origin are a retention in one or both hemispheres of the primitive arrangement of the convolutions natural to the month of fœtal life at which development was arrested. Local defects may be present, such as true porencephaly, which condition is often found in the region of the island of Reil. The lateral ventricles communicate directly with the surface of the brain. Among causes of mal-development are occlusion of cerebral arteries and toxi-infective processes in intra-uterine life.

(2) **Bilateral hemiplegia.**—The degree of paralysis is never symmetrical on the two sides in this form. On one side the hemiplegia is more marked than on the other. All four limbs are spastic. The arms are more affected than the legs and assume the position characteristic of hemiplegia due to a lesion of a middle cerebral artery in the adult. The upper arm is adducted to the chest wall, the forearm flexed and pronated, and the wrist and fingers also flexed. The tendon reflexes are exaggerated, ankle clonus often present, and the plantar responses extensor.

In many cases athetosis, or choreiform movements, appear as the child reaches the age of three years. The involuntary movements affect the limbs chiefly, arms more than legs, but facial grimacing and difficulty in articulating are also common. Rarely a case is seen of pure choreo-athetosis with evidence of pyramidal paralysis either minimal or absent.

The mental functions in this as compared to the preceding type of diplegia are often less impaired, and it is not uncommon, even with athetosis, to find that the intelligence is surprisingly good or normal.

In a large number of such cases it is common to obtain histories of difficult, prolonged, breech and other abnormal forms of delivery, and as might be expected a high proportion occur with primiparæ. A separate group of choreo-athetotics are the survivors of Rh-incompatability with kernicterus (Evans and Polani, 1950).

The bulk of the lesions governing the cerebral birth-paralyses among living infants are the result of *asphyxia* and *anoxæmia*. The subjects of gross intracranial hæmorrhage, if not dead at birth, succumb within a few days or in the ensuing months. Even following the successful removal of an extracerebral hæmorrhage, subdural or extradural, it is common for signs of cerebral defect to persist. The explanation is that mechanical factors capable of producing extracerebral bleeding will almost certainly have given rise to intracerebral lesions as well.

In these paralytics of birth origin the sequence of preparatory events consists during parturition of alterations in external pressure, increase or

sudden release, congestive stasis and asphyxia, leading to local or widespread death of nerve-cells from anoxæmia. "Anoxæmia" covers extreme congestion, œdema and secondary circumscribed petechial hæmorrhages, whereas "hæmorrhage" means gross bleeding due to traumatic laceration of blood vessels. Petechiæ can occur from causes of asphyxiation, or maternal eclampsia, even before labour has commenced.

As Holland has shown, in severe head moulding, breech births, difficult forceps deliveries, the axis of the vein of Galen deviates upwards from its attachment to the straight sinus. The latter is less movable in the relatively rigid tentorium, and a kinking results with progressive venous stasis in the tributaries of the vein of Galen. Schwartz found on microscopical examination following abnormal births that punctate intracerebral hæmorrhagic lesions in the newborn and degeneration and cell-disappearances in infants dying later were preponderantly in the central white substance of the brain and in the basal ganglia—the area of drainage of the vein of Galen and its tributaries. The system of veins draining the cortex are less in the nature of "end-veins," and pass partly to the superior longitudinal sinus and partly to the base of the brain, where it has some connection with the vein of Galen and the lateral or transverse sinuses. The cortical drainage system is less liable to obstruction from mechanical causes during parturition than is the central, based on the vein of Galen. The crude method of production of such asphyxial cerebro-vascular lesions due to mechanical factors at birth explains why they never could be expected to be of equal intensity in the two halves of the brain with resultant symmetrical paralysis. In this connection it is interesting to note that Little's (1862) description was limited to cases associated with a difficult birth, and that he postulated widely spread fine lesions of the cerebral substance which would involve one part of the brain more than another. It is an error to ascribe the title Little's disease to all the forms of antenatal and natal diplegia. Freud also (1897) discriminated between the single and double hemiplegias following difficult births and the symmetrical paralysis of the spastic diplegias.

(3) **Atonic diplegia**—the Foerster type—is much less common than the other types. In it, the hypotonic state of the muscles in infancy resembles amyotonia congenita. In atonic diplegia the tendon reflexes are either normal, reduced, or absent. Development of speech is greatly retarded. As the child gets older and grows in length, the poor state of the muscles of the limbs becomes more conspicuous, contractures are liable to occur, especially of the Achilles tendon, and slight adductor spasms of the thighs with extensor plantar responses may be obtained. The state of the intelligence after several years improves considerably in some cases.

In the atonic type of diplegia the nature of the cerebral defect has not yet been ascertained.

(4) **Cerebellar diplegia,** or congenital cerebellar ataxia. In this type ataxia is noted in early life and there is a tendency to gradual improvement, and it may be to complete recovery, provided evidence of pyramidal paralysis is not co-existent—cerebro-cerebellar paralysis. The children

are late in developing. In attempting to grasp or to move, the infant is said to "tremble." On sitting or standing the body wobbles and overbalances easily. On learning to walk the legs are thrown about in an ataxic manner. Articulation is slow, jerky and monotonous. Nystagmus is a rare rather than a common manifestation.

Anatomically, this form of diplegia depends upon defective development, or on sclerosis secondary to degenerative changes of the cerebellum in intra-uterine life. It has been shown experimentally in animals by Luciani that the symptoms produced by ablation of one lobe of the cerebellum are rapidly recovered from, provided the cerebral cortex is intact; but if the cerebral cortex is injured, then the symptoms produced by removal of the cerebellum persist.

Epilepsy occurs in a small proportion, about two per cent. of all cases of diplegia. Various forms of squint may be observed, an internal strabismus being the most common. Blindness, either cortical or due to optic atrophy, is present in a few cases.

Treatment.—For the muscles and joints, relaxation exercises, passive and active movements, hot baths, and extension splints, will do much to reduce spasm and to prevent and correct deformity. After as much as possible has been accomplished by these methods, tenotomy, tendon stretching and lengthening may be required, but before undertaking the treatment of the severer cases, it is essential to be sure that the mental capacity of the patient is not so defective as to nullify the benefit of the measures employed in overcoming the physical disabilities.

Many cases of cerebral diplegia, especially of the bilateral hemiplegic type, respond well to mental training, and it is often surprising to find quite a high degree of intelligence masked by a slow, sluggish speech, physical awkwardness and ugly choreo-athetotic grimacing. See also reference to Phelps (p. 1517), and to literature of the British Council for the Welfare of Spastics.

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Hemiplegia

The causes of hemiplegia, like those of cerebral diplegia, may be prenatal, natal, and post-natal in origin.

In the prenatal cases, a defect of cerebral development of one hemisphere may be due to an arrest of development, porencephaly, or sclerosis of a cerebral artery. Mental defect is commonly present as well as paralysis.

Hemiplegia of natal origin, mostly in cases of difficult or prolonged delivery, is the result of intracerebral lesions due to asphyxial anoxæmia, or extracerebral hæmorrhage, sub- and extra-dural. Athetoid or choreic

movements develop when the area of damage includes the basal ganglia. Mental defect is less common in this than in the prenatal group of cases. Epilepsy occurs in either group in a number of cases.

Post-natal hemiplegia arises from multiple causes, as from an encephalitis associated with any of the infectious fevers and epidemic encephalitis, also as a complication of diphtheria, infective carditis, chorea, cerebral tumour and abscess, and has occurred during an attack of asthma, or temporarily in migraine (hemiplegic type) and idiopathic epilepsy.

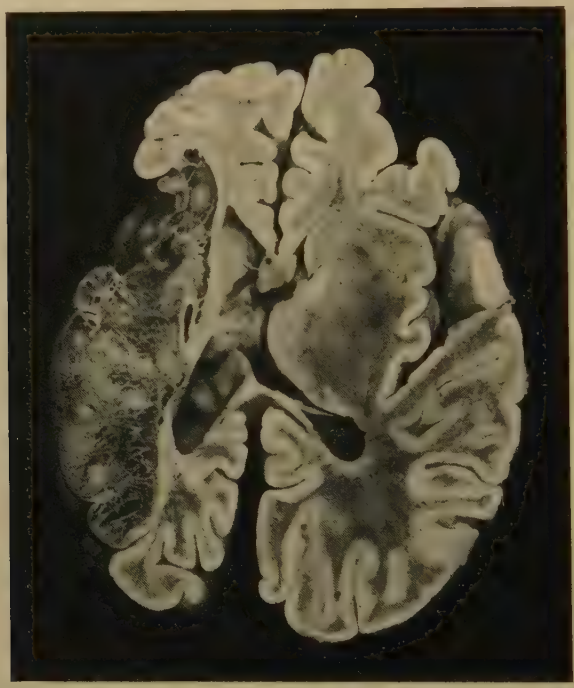

FIG. 382.—INFANTILE HEMIPLEGIA: BRAIN OF AN INFANT, AGED FIVE MONTHS, WHO SUFFERED FROM RIGHT HEMIPLEGIA FROM THE TIME OF BIRTH.

The whole of the cortex supplied by the middle cerebral vessel was in a sponge-like condition. The middle cerebral vessel was represented by a hard cord, but it was impossible to say whether the condition had occurred during intra- or extra-uterine life.

There remains a substantial number of cases seemingly of spontaneous onset, the *acute* or *acquired hemiplegias* of early childhood. A healthy child of normal birth sometimes in the second half of the first year, or in the second, third or fourth year, seldom earlier or later, suddenly without any preceding recognizable form of infection develops convulsions followed by hemiplegia often associated with severe mental impairment. The pathogenesis is obscure, but includes toxic encephalopathy of unknown origin as well as vascular lesions, embolic and thrombotic.

The association of hemiplegia and congenital nævus of the face is not uncommon—Sturge-Weber's syndrome. The cutaneous nævus may cover a wide area of the body on both sides, but is usually well marked and often

limited to the facial area on the side opposite to the hemiplegia. Tortuosity of the retinal vessels is an additional feature of the syndrome, and unilateral buphthalmus. The hemiplegia is usually present at birth, though it may not occur until later. Epilepsy may be a prominent oft-repeated symptom, and mental defect is often present.

Intracranially, a mass of worm-like veins venous angioma —lies superficially in the pia-arachnoid but compressing the cortex, or involves the veins penetrating the brain substance. A partially calcified meningeal

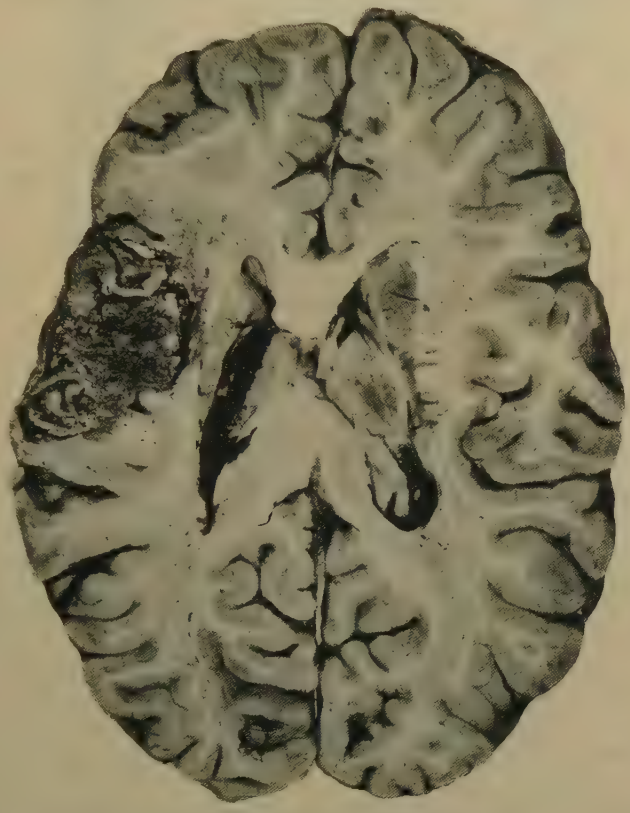

FIG. 383.—BRAIN FROM A CHILD, AGED TEN MONTHS, WHO SUFFERED FROM CONGENITAL MORBUS CORDIS; CEREBRAL THROMBOSIS, POSSIBLY DUE TO AN EMBOLUS, OCCURRED, AND GAVE RISE TO RIGHT HEMIPLEGIA.

angioma on the side of the facial nævus and contralateral to the hemiplegia can be demonstrated by radiography in many cases. In infants before calcification of the angioma has commenced, its presence can be revealed by means of an arteriogram.

SYMPTOMATOLOGY.—In mild degrees of hemiplegia the weakness of the leg alone attracts attention and that of the arms will escape notice unless looked for. The tendon jerks on the affected side are brisker than on the normal side, some unilateral increase of tone can be detected, and the child will pass anything placed in the hand of the affected side to the

FIG. 384.—TRIGEMINAL NÆVUS (CUTANEOUS DISTRIBUTION OF THE OPHTHALMIC DIVISION OF THE RIGHT FIFTH NERVE), IN A BOY, NINE YEARS NINE MONTHS, WITH EPILEPSY, LEFT HOMONYMOUS HEMIANOPIA AND WEAKNESS LEFT HALF OF BODY.

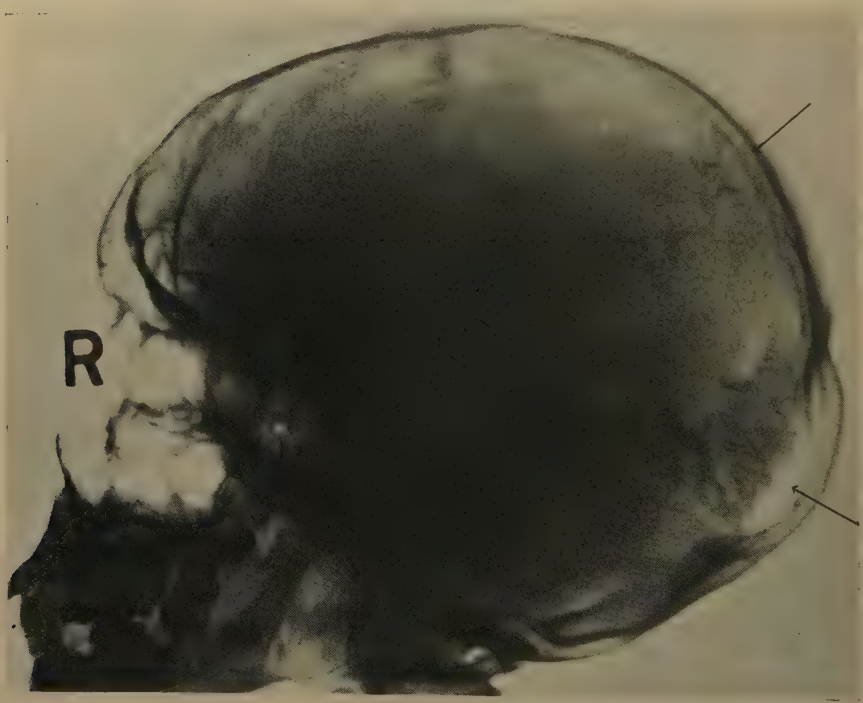

FIG. 385.—X-RAY SHOWING HOMOLATERAL PIAL ANGIOMA (CALCIFIED).
(Dr. Maitland-Jones's case, by courtesy of the Proc. roy. Soc. Med., London.)

other or normal hand. As the child increases in stature scoliosis develops from diminished growth of the weak leg.

TREATMENT.—By games and exercises the child must be encouraged to develop the use of the weak hand. Raising the sole of the shoe on the hemiplegic side is essential to prevent a scoliosis developing.

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INTRACRANIAL TUMOUR

Frequency, sex and age.—Various tables on the frequency of intracranial tumour in childhood closely support Cushing's figures of one in childhood to about six in adult life, or 154 preadolescent cases out of 1,100 verified cases at all ages. The sexes are equally affected. Numerous authors have placed the years six, seven and eight as the age in childhood of highest incidence, but cerebral tumour is not uncommon in infancy and has even been found in the still-born. Stern's study of 102 cases, diagnosed between 1921 and 1935 at Great Ormond Street, showed fifty-five cases under five years of age and forty-eight between the ages of five and twelve years.

Situation and duration.—Sixty to seventy per cent. of the tumours in children are subtentorial. Here the commonest situation is mid-line cerebellar growing from the roof of the fourth ventricle, less often lateral cerebellar or pontine and rarely in the medulla. The next biggest group occurs in the diencephalic or midcentral region (Marburg—30 per cent.) including those in the floor of the third ventricle, the suprasellar and the paraventricular arising between the lateral wall of the third and the mesial wall of the lateral ventricle, and those in the pineal area. Tumours of the hemispheres come third in frequency. Growths of the choroid plexuses are rare.

TABLE 51

	Cerebellar	Diencephalon	Hemispheres	Pontine	Lateral ventrical
Stern : (56 verified cases ; ages, birth to 12 years)	32	8	9	7	0
Smith and Fincher : (87 cases ; ages, 13 months to 15 years)	51	13	16	4	3

The duration of symptoms has little if any relation to type, benign or malignant, of the tumour, and site can be as potent a factor promoting death as malignancy, as for instance a benign type of growth in the pons.

Types of growth.—In children, gliomas at 75 to 80 per cent. outnumber other types. They are subdivided into astrocytomas and ependymomas—benign types, and medulloblastomas and spongioblastomas—malignant types. The first three types most commonly arise in the cerebellum and fourth ventricle. In seven pontine growths six were benign astrocytomas (Stern). The spongioblastoma multiforme, or

malignant glioblastoma multiforme, is mostly a tumour of adult life and of the hemispheres, but is found also in children. The next commonest genus in children are the suprasellar tumours of Rathke's pouch composed of mixed epithelial and glial tissues, often with areas of degeneration, cyst formation, and calcification. Tumours of the pineal area are atypical teratomas, gliomas, cysts and the rare pinealoma. Pituitary adenomas, acoustic neurinomas and meningiomas rarely occur in children under twelve years of age. Occasionally sarcomas and hæmangioblastomas are met with.

Tumours are called *congenital*, or also *diverticular*, that originate from disturbances of cerebral development in fœtal life, and arise chiefly in the region of pouch-outgrowths and canals ; *e.g.* Rathke's pouch tumour, pineal tumour, gliomas of the optic nerve, and some gliomas arising from the central canal of the cerebellum.

Calcification of a cerebral tumour in a child occurs most often in the suprasellar craniopharyngioma. When absent, this type of tumour is difficult to differentiate from a paraventricular glioma. Calcification may occur in a pinealoma, and in an ependymoma, which usually has a ventricular origin but may be extraventricular.

Tuberculomas are not common. Van Wagenen (1927) states that *macroscopical* tuberculomas were found nine times only (9·1 per cent.) in ninety-eight cases of tuberculous meningitis.

General symptoms.—In the young child the skull accommodates more readily to increased intracranial pressure by opening of the sutures with enlargement of the head, so that the cardinal symptoms, headache, vomiting and papilloedema, may be inconspicuous and unduly late of onset. In general, however, early symptoms are headache, chiefly frontal, nausea and repeated vomiting, which are often dissociated and the latter unrelated to the taking of food, enlargement of the head with easily palpable sutures, ocular palsies, nystagmus and failing vision, disturbances of gait and of the use of the hands. Convulsions seldom occur, as tumours of the hemispheres are uncommon. Focal signs, such as developmental and metabolic disorders and somnolence associated with the paraventricular (third) tumours, and the sprightliness of the case of early cerebellar neoplasm, will be mentioned under the appropriate localizations. It often happens that the secondary signs of raised intracranial tension caused by a space-occupying lesion, or the hydrocephalus produced by the blocking of the iter or of a ventricle, obscure or swamp the true signs of localization. False localizing signs are paralysis of the sixth nerve, drowsiness increasing to coma, increasing rigidity often with bilateral extensor plantars and tremors of the limbs. Successful localization often depends as much upon obtaining a carefully detailed history of the early symptoms as upon the examination of the child. In many cases no sure localization is possible without ventriculography.

A common sign of increased intracranial tension due to obstructive hydrocephalus in children is obtained on tapping the skull, namely the crack-pot note, like the sound of tapping a ripe melon.

X-ray photographs reveal opening of the sutures, thinning of the bones of the vault of the skull giving the appearance of " thumb-

printing," or the "mackerel-sky" sign. This latter appearance taken alone is often present in the skulls of normal children, but in conjunction with widening of the pituitary fossa and atrophy of its clinoid processes indicates chronic obstructive hydrocephalus.

Conditions which may resemble cerebral tumour clinically are meningitis, especially of a slowly progressing tuberculous type, cerebral abscess and encephalitis lethargica. Examination of the cerebro-spinal fluid helps to differentiate them (for C.S.F. in cerebral tumour, see page 1206). In the early stages periodic or cyclic vomiting is often diagnosed erroneously for intracranial tumour.

Tumours of the cerebellum.—As most cerebellar tumours in children are mesially placed, the signs peculiar to the locality are fairly evenly distributed on the two sides of the body; when the growth is unilateral the signs are most pronounced on the same side. The characteristic features are (1) ataxy, (2) hypotonia, (3) errors of posture and locomotion, and (4) nystagmus and ocular paralyses. The cranial sutures widen early as the fourth ventricle is soon blocked by the growth with resulting obstructive hydrocephalus. The mental habit of the child with cerebellar tumour is at first often bright, almost precocious, in contrast with the somnolence produced by a neoplasm growing in the floor of the third ventricle. Papilloedema develops early and is usually considerable, 4 to 6 D+, but there are exceptions where it has not developed even up to the date of operation though vision may be failing. With increasing intracranial pressure the cerebellar tonsils and medulla are jammed down into the foramen magnum and pyramidal signs, spasm, tremors, even rigidity, extensor plantars, intermingle with and obscure the genuine signs of a cerebellar lesion.

FIG. 386.—PHOTOGRAPH OF A CHILD, ILLUSTRATING THE POSITION OF THE HEAD ASSUMED IN SOME CASES OF CEREBELLAR DISEASE.

The position seen in the photograph would indicate a lesion of the left lateral lobe of the cerebellum.

Ataxy.—The power of muscular co-ordination is diminished or lost on both sides of the body if the tumour is mid-line, on the same side as the lesion when unilateral. Inco-ordination is more conspicuous in the arm than in the leg or spinal muscles. The disability depends upon asynergia of the muscle contractions which go to make up a voluntary movement, and also upon a defect in reflex muscle tone. Ataxy occurs only on active movements of the limbs, and is manifested by a coarse rather slow tremor of wide excursions. It is elicited in the arm by means of the finger-nose test, and in the leg by getting the patient to draw a line with one heel down the shin-bone from the knee of the other leg. When asked to touch objects his finger falls short or overshoots the mark—dysmetria. He cannot carry out in rapid succession move-

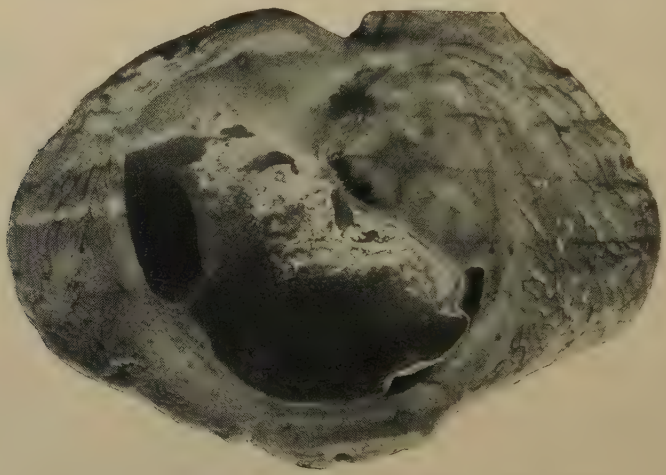

Fig. 387.—Cystic Tumour of the Mid-Lobe of the Cerebellum.

The cyst is filled with a yellow viscid fluid, and arises in connection with a glioma. Note the compressed condition of the pons below the cyst.

ments of antagonistic muscles, as in alternate pronation and supination of the hands—dysdiadochokinesia.

Hypotonia.—Loss of tone in the muscles is always present, but may be masked in the later stages by the signs of a general increase of intracranial pressure. The postural tone of the muscles is inhibited, and in active movement the normal after-contraction (reflex muscle tone) of the muscles which antagonize those employed in producing the movement is reduced or delayed. The laxity of the muscles is noticeable in the degree to which the limb can be over-extended at the various points. Actual muscular weakness is not present at first.

Posture and gait.—With a tumour laterally placed, the head is often deflected to one side, so that the occiput approaches one shoulder and the chin is turned towards the opposite side. A backward inclination of the head is sometimes seen when the tumour is in the vermis. Sitting in bed, the patient may require the support of one or both arms to prevent himself toppling over. The gait is of a broad-based reeling type

with staggering towards the side on which the cerebellum is most affected. Giddiness is complained of by older children.

Ocular paralyses. Bilateral nystagmus with larger and slower excursions on directing the eyes towards the side of the lesion is an important sign of a unilateral lesion. When the growth is in the midline without lateral spread to the dentate nuclei in the hemispheres, nystagmus is variable, intermittent, or absent. A weakness of conjugate movement in holding the gaze fixed to an object placed laterally is a more constant sign; the eyes swing back to central position involuntarily. Palsy of the external rectus muscle is common, but has no localizing value.

Reflexes.—The state of the tendon jerks is either normal, diminished, or abolished.

C.S.F.—Lumbar puncture must only be done for diagnostic purpose with great care, slowly removing only 1 c.cm. or, by greater or rapid removal, the medulla may be plugged into the foramen magnum with fatal results.

Extracerebellar, or acoustic nerve tumours—neurinomas—have occurred in children in association with generalized neurofibromatosis. Familial bilateral tumours of the acoustic nerve have been described, the onset of the symptoms in some of the cases being in childhood.

The cerebellar signs are unilateral in the case of a single acoustic nerve tumour. As the tumour lies in the cerebello-pontine angle at the exit of the seventh and eighth nerves, they become affected giving rise to facial paralysis and nerve deafness on the side of the lesion. The fifth also may be involved, as shown by anæsthesia on the side of the face and weakness of the muscles supplied by the nerve. On the same side the sensation of taste may be lost over the half of the tongue, or its anterior two-thirds.

Cerebellar angioblastoma is a highly vascular tumour composed of a fœtal type of vessel-forming cell. Of small size itself, it commonly gives rise to cystic formations in its vicinity filled with a yellow albuminous fluid. Associated abnormalities in other organs are common—Lindau's disease—such as, angioblastoma of the retina, cysts of the pancreas and kidneys, and hypernephroma of the adrenal.

Tumours of the cerebral hemisphere.—Tumours of the frontal and fronto-parietal are more common than those of the temporal or occipital lobes. Besides those developing in the substance of a hemisphere, others starting from the wall of a lateral ventricle, as ependymomas, may reach the surface of the brain.

A tumour of a frontal lobe usually gives rise to a hemiplegia of gradual onset, with weakness commencing in face, arm, or leg, according to its position. There may also be aphasia when the tumour is on the left side in a right-handed child. Epilepsy is an important symptom. The fits may occur when the tumour is situated at the cortex, or from cortical irritation of a subjacent growth. Subsequent to a fit, the degree of paralysis is often increased.

When the tumour extends, or is situated behind the fissure of Rolando, hemi-anæsthesia may result, and a deeply seated lesion involving the

posterior part of the internal capsule will give rise to hemiplegia, hemianæsthesia and hemianopia. The skull must in all cases be carefully examined, as a local elevation with softening of the bone may occur immediately over a tumour involving the cortex.

FIG. 388.—PHOTOGRAPH OF A CHILD, SHOWING BILATERAL PTOSIS AND EXTERNAL STRABISMUS DUE TO A LESION IN THE REGION OF THE CORPORA QUADRIGEMINA, DESTROYING THE NUCLEUS OF THE THIRD NERVE.
The position of the tumour is seen in fig. 389.

Tumours of the diencephalic or mid-central region can occur in infancy, giving rise to few symptoms beyond expansion of the skull from ventricular dilatation. Papillœdema does not begin until the neoplasm is well developed, as the ease with which the sutures open readily compensates for the increasing intracranial pressure. In older children, tumours in this area are localized both by focal signs of paralysis and by the presence of developmental and metabolic disorders.

FOCAL SIGNS.—Ocular paralyses are a prominent feature when the third ventricle, corpora quadrigemina, or crus are involved. The pupils are usually dilated, often unequal, and may be inactive to light but

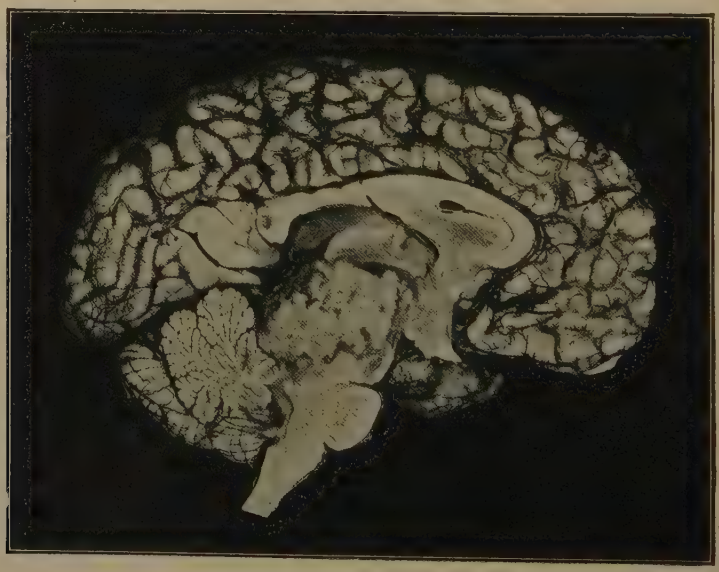

FIG. 389.—VERTICAL SECTION THROUGH BRAIN, SHOWING TUMOUR IN REGION OF THE CORPORA QUADRIGEMINA.
(Compare with fig. 394, tumour of the pons.)

react on accommodation, or inactive both to light and accommodation. Interference with the third nerve or its nucleus in the crus gives rise to ptosis, external squint from paralysis of the internal rectus muscle, or paralysis of all the muscles of third nerve innervation. A combined lesion of third nerve and red nucleus can give rise to ophthalmoplegia on the side of the lesion and rhythmical tremor of the contralateral limbs. A tendency to fall backwards has occurred with involvement of the red nucleus. Interference with the corpora quadrigemina causes defective upward and downward movements of both eyes. Failure of vision occurs early, the discs often show signs both of pressure atrophy and moderate papillœdema from general intracranial hypertension. At

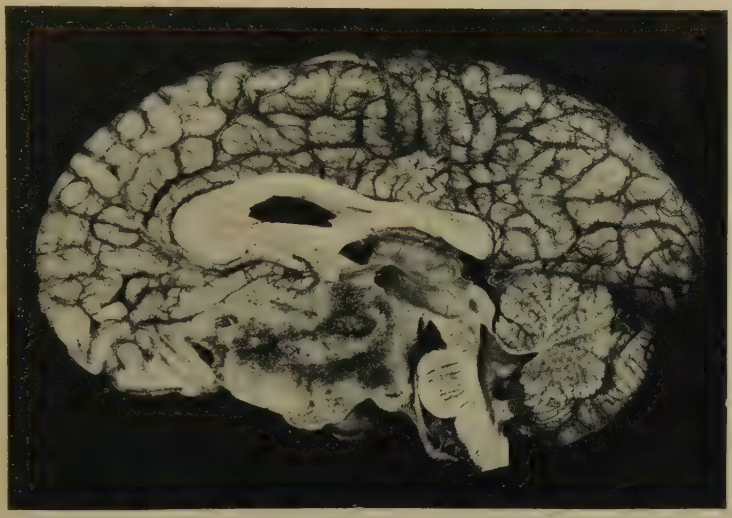

FIG. 390.—PHOTOGRAPH OF A SUPRA-PITUITARY TUMOUR (ADAMANTINOMA). THE INITIAL SYMPTOMS, FAILURE OF VISION, OCCURRED THREE MONTHS BEFORE THE DEVELOPMENT OF ANY OTHER SIGN OF THE DISEASE. THEN THE USUAL SYMPTOMS OF INTRACRANIAL PRESSURE DEVELOPED, WITH LOSS OF DEEP REFLEXES.

The child died seven months after the initial symptom. The pituitary body was unaffected.

a later stage, downward pressure upon the posterior fossa often produces cerebellar signs. Pressure on the pyramidal tracts causes signs of hemiplegia or diplegia to appear. Hydrocephalus above the level of the iter develops early.

DEVELOPMENTAL AND METABOLIC DISORDERS. -These comprise infantilism and sexual regression with obesity, or the opposite, gigantism or precocious puberty and muscular development. It is doubtful whether the pineal itself has an active secretion in the production of *macrogenitosomia præcox*. This syndrome can occur with neoplasms encroaching anteriorly, inferiorly, as well as posteriorly upon the third ventricle. It is more probable that variations in degree and extent of interference with the hypophysis and its connection in the floor of the third ventricle underlie the different syndromes. Polyuria and polydypsia—diabetes

insipidus—occur in some cases of tumour in this region. Other signs of pressure upon or involvement of the tuber cinereum and pituitary are somnolence, obesity, and hyperglycæmia and glycosuria. X-rays show that erosion, flattening and widening of the pituitary fossa and internal hydrocephalus occur early in this group of cases.

(1) The suprapituitary adamantinoma or craniopharyngioma of congenital origin gives rise to symptoms in childhood or in adult life. Beginning early, the child retains an infantile appearance, is fat, somnolent, and the skull gradually enlarges; in cases of onset after puberty, sexual regression with obesity occurs.

These neoplasms develop from cell residues derived from the fœtal cranio-pharyngeal duct. Early in fœtal life two diverticula grow toward each other and meet, one, Rathke's pouch, is an invagination of the surface ectoderm of the bucco-pharyngeal cavity, the other is a down-growth from the floor of the primitive fore-brain. From the former is developed the pars anterior and the pars intermedia of the pituitary, while the latter gives rise to the pars posterior or nervosa and to the infundibulum. The buccal invagination is the source of a thin layer of epithelial cells which spreads over the anterior surface of the infundibulum as far up as the floor of the third ventricle, and sometimes forward towards the optic chiasma. Erdheim found that collections of these epithelial cells could be demonstrated at two points in particular, at the upper and lower ends of the anterior aspect of the infundibulum. These are the two situations at which the suprapituitary tumours originate. They are indolent in growth, having phases of dormancy and renewed activity. In the case of a girl, the symptoms began in the fourth year and the child was alive at fifteen, though four years previously intense vomiting and headaches followed by coma suggested a period of active growth.

The *clinical features* are the outcome of pressure upon neighbouring structures, the optic chiasma, the pituitary, and the floor of the third ventricle. Visual defects, adiposity and drowsiness are the most characteristic symptoms.

Headache between the eyes is often severe. The child has an infantile appearance, a fine skin well padded with subcutaneous fat, growth is retarded, the features are small and delicate, the fingers short and tapering, and at puberty signs of sexual maturity do not appear.

Characteristic visual defects are bitemporal, quadrantic, or homonymous hemianopia according to the site at which the tumour exerts pressure upon the chiasma or optic tracts. A tumour originating at the upper end of the infundibulum commonly presses downwards and forwards upon the chiasma, producing at first bilateral quadrantic defects in the lower halves of the visual fields. Conversely, a tumour growing at the lower infundibular area will press upwards from behind on the chiasma giving rise to bilateral quadrantic defects of the upper halves of the visual fields. Diplopia is a symptom of common occurrence. The state of the discs may show several dioptres of swelling in one or both eyes, or a primary optic atrophy.

These patients commonly exhibit an increased sugar tolerance, and the rise and fall of the blood sugar following a glucose meal is delayed. Abnormal thirst and excessive micturition have been recorded.

Radiography shows a wide flat sella turcica, and in older children irregular shadows denoting calcification in the growth are often visible in the suprapituitary region.

(2) The pituitary adenomas rarely occur in childhood, but a possible cause of gigantism might be a chromophil adenoma. More often over-action of acidophil cells without tumour formation appears to be the cause.

(3) The pineal-area tumours and those of the hypothalamus, or floor of the third ventricle, sometimes give rise to pubertas præcox and to diabetes insipidus, together or separately.

Pineal area tumours occur in both sexes, but have given rise to the syndrome of macrogenitosomia præcox in boys only. Among sixty cases of pineal tumour collected by Bailey and Jelliffe, twenty occurred before puberty and seven of these showed precocious puberty. In a series of twelve cases reported on by Horrax and Bailey, five occurred before puberty with two showing precocious puberty. The precocious development is manifested in the following ways: rapidity of growth with advanced epiphyseal ossification, appearance of adult muscularity, often some degree of obesity, large genitalia, axillary and suprapubic hirsuties, gruff voice, and in some cases a sexually awakened mentality.

Tumours in the floor of the third ventricle can also give rise to pubertas præcox, usually at an early age. Gross states that either sex may be affected and gives the signs as follows: genital enlargement, appearance of secondary sex characteristics, mental and physical, excessive somatic development, advancement in epiphyseal development, and possibly either oliguria or polyuria.

Diabetes insipidus is a symptom in a few of these cases of tumour in the area of the pineal and hypothalamus. Fluid intake amounts to sixteen or more pints daily with output one or

FIG. 391. –BOY, AGED EIGHT YEARS, WITH DIABETES INSIPIDUS, PRECOCIOUS PUBERTY, ADULT CONFIGURATION, SCARCITY OF FAT.

Compare with following fig. to note site of tumour.

(Both pictures by courtesy of Editors, Proc. roy. Soc. Med.)

two pints less. The children become water-addicts and bed-wetting is common. They respond to pitressin therapy in the same way as the idiopathic cases do (Wyllie, 1943).

With tumours in either of the regions described, signs of raised intracranial pressure are often late to appear up to several years after precocious puberty or diabetes insipidus have been present. A neoplastic connection is suggested by development of inequality of the pupils, paralysis of conjugate upward movements of the eyes, due to pressure effect upon the superior corpora quadrigemina, onset of headache, disturbances of vision, and radiographic evidence of internal hydrocephalus.

Fig. 392.—Tumour in the Region of the Pineal Gland.

Proved to be a benign glioma.

The blood pressure in these cases is not usually raised, whereas it is in most cases of hypernephroma with pubertas præcox.

Cases of pubertas præcox caused by cerebral tumour have to be distinguished from those due to virus encephalitis and syphilitic meningo-encephalitis affecting the hypothalamus and from tumours of the adrenal cortex and testis. The sterones, chiefly androsterones, in the urine in the adrenal cases are commonly abnormally high, 840 units or so in twenty-four hours (the normal being below 10 in children), whereas they are unaffected or moderately increased with cases of cerebral neoplasm. Similarly, the neoplastic cases of diabetes insipidus have to be differentiated from those due to midbrain encephalitis, or that occur as a sequel to fracture through the base of the skull, or that are "idiopathic" (see endocrine disorders).

Tumours of the pons and medulla.—Tumours of the pons usually

cause early paralysis in one or more cranial nerves. Exceptional cases are met in which in spite of the size of the tumour hypertrophy of the pons—paralyses only occur at a later stage. Early manifestations of a

FIG. 393.—PHOTOGRAPH OF A BOY, SHOWING SQUINT PRODUCED BY WEAKNESS OF THE RIGHT EXTERNAL RECTUS, AND RIGHT FACIAL PARALYSIS DUE TO A TUMOUR OF THE PONS.

The position of the tumour is seen in fig. 394.

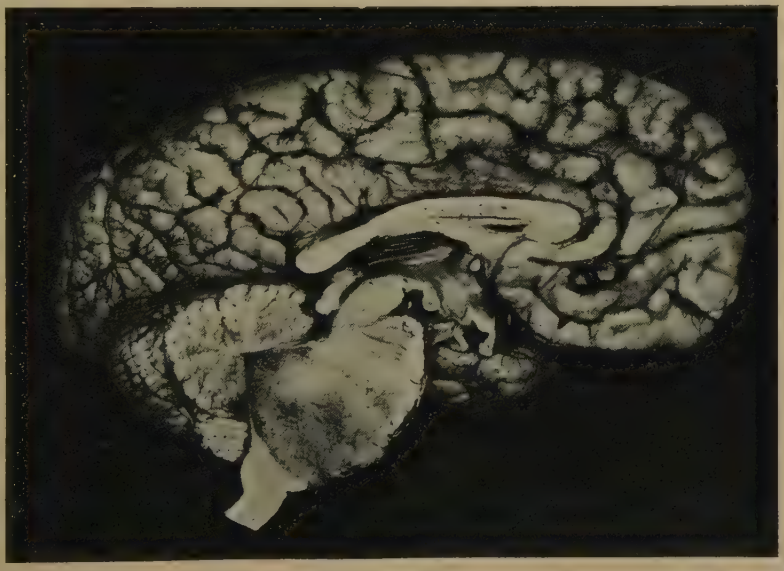

FIG. 394.—VERTICAL SECTION THROUGH BRAIN, SHOWING NEW GROWTH INVADING THE PONS.

The tumour produced at first squint and paresis of the right side of the face and left side of the body. Optic neuritis was never present. (Compare fig. 389.)

pontine tumour are squint from paralysis of one or both external recti, a hemiparesis of one side and a facial paralysis of the opposite, a crossed paralysis. The facial paralysis is usually of the peripheral or lower neuron type affecting forehead, eye and lower face. The fifth nerve is liable to be involved in both its motor and sensory portions. A diminution or absence of the corneal reflex is an early sign and can be demonstrated before any analgesia is detected.

With both halves of the pons involved, there may be signs of cerebral diplegia with much rigidity and opisthotonos, these symptoms being due either to direct affection of the pyramidal tracts in the pons, or to hydrocephalus following blocking of the iter of Sylvius. It is unusual for anæsthesia of the trunk to be present in cases of pontine tumour, but ataxy is common owing to involvement of the cerebellar peduncles.

Tumours of the medulla are rare and so closely related to pontine tumours that there is no clear line of separation. The seventh to twelfth nerves are specially liable to be affected, causing facial paralysis, nerve deafness, paralysis of the palate and constrictors of the tongue, of the sternomastoid and upper portions of the trapezius muscle, and of the vocal cords.

Papillœdema is specially late in developing in cases of pontine tumour. In cases of glioma of the pons observed over a period of six months, no swelling of the discs occurred up to the time of death.

Tumours of the choroid plexus are rare and difficult to localize. The clinical picture resembles a post-basic meningitis with frequent vomiting, headache, a staring vacant expression, photophobia, neck stiffness, possibly a squint, and an expanding skull. In a male infant of nine months with a bulging fontanelle and the above symptoms, the cerebral-spinal fluid was under a pressure of over 300 mm.; clear, protein 30 to 150 mgm. per 100 c.cm., pleocytosis of 61 to 170 per c.mm. chiefly lymphocytes. Up to the date of death repeated lumbar punctures relieved this symptom temporarily.

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Treatment

The main object in all cases of proven intracranial tumour should be total extirpation wherever the lesion is benign in character, accessible in situation and is invading no vital structure. In view of the relatively high incidence of tumours in the posterior fossa (the common site for intracranial tumour in the young) and the fact that about 50 per cent. of such lesions are benign gliomas, the field for neurosurgery is a wide one.

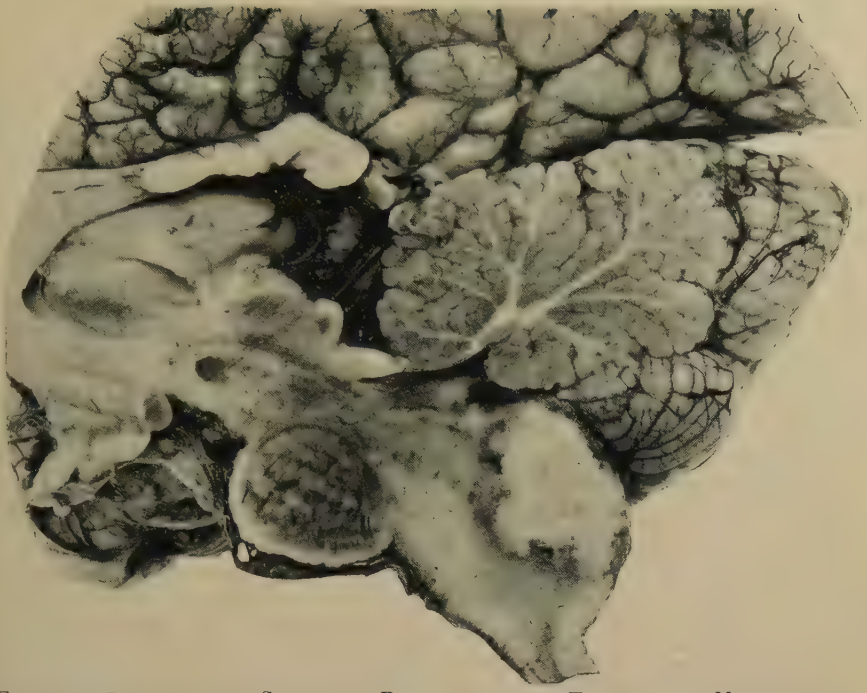


FIG. 395.—LONGITUDINAL SECTION OF BRAIN, SHOWING A TUBERCULOUS MASS SITUATED IN THE MEDULLA, AND INVOLVING THE PEDUNCLE OF THE CEREBELLUM.

Forced movements of rotation in the direction of an outgoing corkscrew were in the early stages of the disease the most prominent symptom.

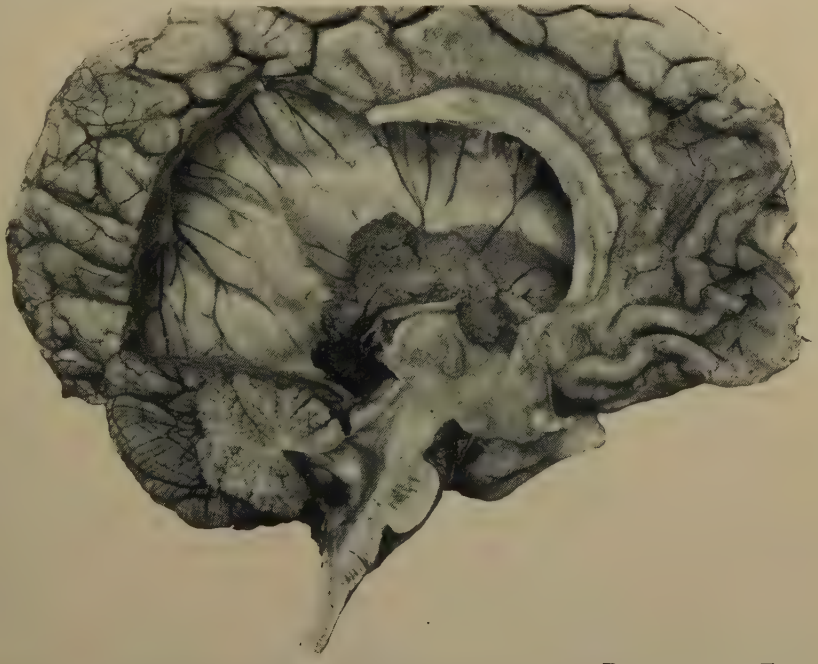


FIG. 396.—HYDROCEPHALUS STARTING THREE MONTHS AFTER BIRTH, DUE TO TUMOUR OF THE CHOROID PLEXUS.

The choroid plexus weighed 65 grammes; the normal plexus weighs 0·78 gramme.

It is, in fact, fair to say that the results of operative excision of intracranial tumours in children form some of the most brilliant achieved in this branch of surgery.

The preliminary essentials to successful treatment are careful neurological examination (both from the point of view of accurate localization of the lesion and for the purpose of assessing the post-operative result), adequate X-ray photographs of the skull and a satisfactory ventriculogram. Only by the consideration of the information derived from these three sources, combined with a detailed and thorough history of the ailments of the child, can the information be obtained necessary to plan the correct operative procedure.

It should be emphasized that a serious attempt should be made to pre-determine not only the exact location of the lesion but also its probable histological character.

Ventriculography should never be omitted as a final investigatory measure, for the clinical localization of tumour is all too often at fault and not infrequently in some important detail. Whilst it is a golden rule in neuro-surgical intervention in adults to proceed with craniotomy as soon as the ventriculograms are available, certain modifications in this course have often to be made when dealing with children. It is usually possible to perform ventriculography under local anæsthesia in girls from the age of five years upwards but, in boys, few will tolerate the procedure before the age of eight. Below these ages, therefore, it is necessary to use general anæsthesia both for the operation and the subsequent radiological manipulations : it is consequently undesirable to carry out the major operation on the same day as the ventriculogram for this would involve the administration of two general anæsthetics in one day.

When an operable lesion is disclosed by ventriculography it is advisable to tap one lateral ventricle immediately after the ventriculograms have been obtained, thus reducing the intracranial pressure and tending to avoid the serious consequences which may follow the disturbances of intracranial circulation associated with the performance of ventriculography. Repeated ventricular puncture or continuous drainage may be needed to tide the child over the next two days when it would be reasonable to give a second general anæsthetic and proceed with operative removal of the tumour.

Opinions vary as to the desirability of premedication : it is the authors' practice to avoid all drugs used for such purposes for most have some depressant action upon the medulla, the functions of which are all too often impaired by the mere existence of the raised intracranial pressure produced by the neoplasm. A suitable dose of atropine is all that is required, followed by gas, oxygen and ether anæsthesia administered by endotracheal tube. This latter method is most desirable. Alarming changes in respiratory rhythm and rate are of common occurrence when operating in the vicinity of the medulla in children and it is of great assistance to be able to control at short notice the gaseous exchange in the lungs which this mode of anæsthesia renders possible.

During the introduction of anæsthesia a cannula should be inserted into one internal saphenous vein and a glucose saline drip started. Whilst helping to maintain the general condition of the child this precaution enables a blood transfusion to be given should any sudden calamity take place or the blood pressure slowly decline to an unsafe level consequent upon a prolonged or difficult operation.

During the course of operation the blood pressure, pulse rate, respiratory rhythm and temperature should be charted at frequent intervals so that due warning may be given to the surgeon of serious change in the condition of the patient.

Manipulations in the subtentorial chamber frequently produce sudden and striking changes in blood pressure, pulse and respiration, and suspending the operation for a few minutes may often be sufficient to permit a return to normal. It should be the duty of the anæsthetist to keep the surgeon informed of any change in the condition of the child and to institute appropriate remedial measures.

It is not proposed to deal with the details of surgical technique for these differ in no way from the methods in use in adult neurosurgery. It might well be said, however, that prolonged operations should be avoided, particularly in the smaller children. It is usually possible to divide an operation into several stages: for example, in the removal of a large cystic astrocytoma of the cerebellum, the first stage would be a suboccipital decompression with tapping of the cyst through the intact dura, the second stage being the opening of the dura and removal of the tumour or, if the condition of the child were still poor, the second stage might again be subdivided into two. Firstly the dura would be opened and the cyst again tapped, whilst at a third operation the wound would be re-opened and the tumour totally excised. This reduces each operation to a relatively short time and, in the authors' hands at any rate, would appear to lower the mortality rate, although at the expense of an increase in the duration of stay in hospital.

Stress might also be laid upon the fact that surgery of this nature and severity can only be successfully carried out by a team of persons skilled in the art and constantly used to its practice.

Situation and pathology

In an unselected series of fifty verified intracranial tumours seen during an eight-year period there were thirty-one subtentorial and nineteen supratentorial lesions:

Subtentorial		*Supratentorial*	
Medulloblastoma	16	Craniopharyngioma	6
Astrocytoma	11	Malignant glioma	3
Pontine glioma	2	Meningioma	3
Ependymoma	1	Astrocytoma (cystic)	2
Astroblastoma	1	Oligodendroglioma	1
		Malignant papilloma	1
		Pinealoma	1
		Pituitary adenoma	1
		Osteoclastoma	1
	31		19

Results of operation

Of these fifty cases forty-seven were operated upon with nine deaths in the post-operative period (duration of stay in hospital), giving an operative mortality rate of 19 per cent. At the present time twenty-eight of the forty-seven cases are alive, and of these twenty-eight, twenty-four are well and able to enjoy life, attend school or work normally. Of the twenty-four who are well, a few only show abnormal physical signs, but ten will inevitably have recurrence of growth at some future date owing to the pathological nature of the lesion. Fourteen cases thus remain of the forty-seven operated upon in whom total extirpation of the tumour was carried out and in whom no recurrence need be expected, the time since operation varying from a few months to eight years.

From this series of fifty cases, therefore, it can be said that the rate of cure is twenty-eight per cent. (fourteen cases of fifty) and the operative mortality 19 per cent., whilst 28 per cent. will be improved by operation for periods varying from a few months to nearly five years (to date). The fourteen cases considered cured who may reasonably have the expectation of life of a normal individual consists of nine cases of astrocytoma (seven subtentorial and two supratentorial), one case of pituitary adenoma, two of meningioma, one of osteoclastoma and one of craniopharyngioma.

Mortality

Of the nine post-operative deaths no less than six occurred in cases where the existing state of internal hydrocephalus had not been relieved by the operative procedure. Three cases of medulloblastoma in the posterior fossa had only a suboccipital decompression performed, no attempt having been made to remove the growth with consequent persistence of obstruction to the flow of cerebro-spinal fluid from the third ventricle. One pontine glioma, one pinealoma and one meningioma (the latter a midline lesion growing from the occipito-sphenoid region) were all irremovable and producing internal hydrocephalus. Of the remaining three deaths two occurred in children with large astrocytomas of the posterior fossa where undue disturbance of the medulla was produced by the surgical manipulations required for their removal. The ninth death followed the attempted excision of a craniopharyngioma when severe damage was done to the floor of the third ventricle and death from hyperpnœa and hyperpyrexia soon supervened. It is thus seen that failure to relieve an existing internal hydrocephalus or damage to the vital centres in medulla or hypothalamus are the common causes of post-operative death.

ENCEPHALOGRAPHY AND VENTRICULOGRAPHY

In the investigation of many forms of intracranial disease a visible definition of the ventricular and subarachnoid spaces proves of the greatest value. The contrast medium in common use is air, although other gases have been employed.

The usual methods employed are: ventriculography in which air is introduced directly into the ventricles through one or more post-parietal burrholes, and encephalography in which air is injected into the sub-arachnoid space by cisternal or lumbar puncture.

Each method has its indications: ventriculography in cases of space occupying lesions, either chronic or acute and in certain cases of acute cranio-cerebral injury, whilst encephalography is employed where evidence of increased intracranial pressure is absent; in such conditions as degenerative disease, developmental anomalies and the sequelæ of head injuries.

Cisternal encephalography.—Under local anæsthesia with the patient sitting up a fine bore needle is inserted in the midline of the neck at the level of a line joining the tips of the mastoid processes when the head is held flexed with the chin drawn in. The needle is first made to strike the region of the posterior margin of the foramen magnum and is then worked gently downwards until no bony resistance is encountered; deeper introduction of the needle will then cause it to pass through the ligaments between the occiput and atlas and finally the theca. On withdrawing the stylet fluid will usually drip slowly from the needle or may require to be aspirated with a syringe. For each 5 c.cm. of cerebro-spinal fluid obtained 5 c.cm. of air are injected. About 20 to 40 c.cm. of air injected are generally adequate to produce ventricular filling.

During the injection, and particularly if the air is entering the sub-arachnoid space rather than the ventricles, severe headache, nausea, vomiting and fainting may occur, and this method is mainly used in the older children with ages ranging from twelve to sixteen years. Filling of the ventricles is obtained in about eighty to eighty-five per cent. of cases.

Lumbar encephalography.—In children this procedure is carried out under general anæsthesia as severe headache and vomiting will otherwise occur and co-operation will not be obtained. With the patient anæsthetized and in the sitting position two lumbar puncture needles are inserted in the lower lumbar region and the stylets withdrawn. Cerebro-spinal fluid will flow freely and each 10 c.cm. withdrawn are replaced by air injected with a syringe. All the cerebro-spinal fluid which will come away is replaced and more than 200 c.cm. can be obtained in quite small children where there are gross abnormalities of the intracranial contents. When the flow of cerebro-spinal fluid appears to be stopping the head is shaken after which a further flow may be produced as the result of the freeing of an air lock.

The ventricles fill in about 70 per cent. of cases by this route, but better filling of the subarachnoid space is achieved than when employing the cisternal route. It is therefore particularly applicable in children suspected of extensive cortical atrophy and gross developmental abnormalities where it is desired to reveal the contours of the cerebral cortex itself.

Ventriculography.—This minor operation is carried out preferably

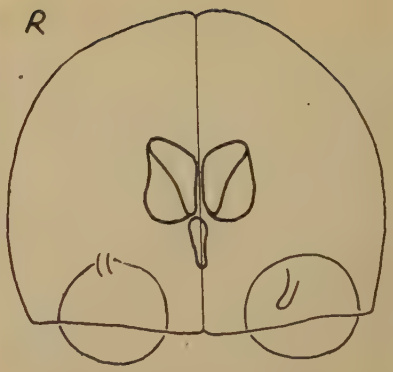
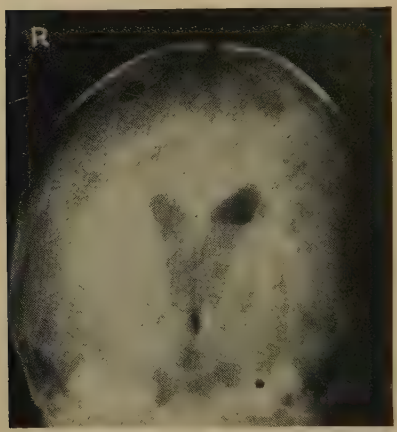


FIG. 397.—NORMAL ANTERO-POSTERIOR VENTRICULOGRAM SHOWING SYMMETRICAL LATERAL VENTRICLES, MIDLINE THIRD VENTRICLE AND SMALL AMOUNTS OF AIR IN THE TEMPORAL HORNS.



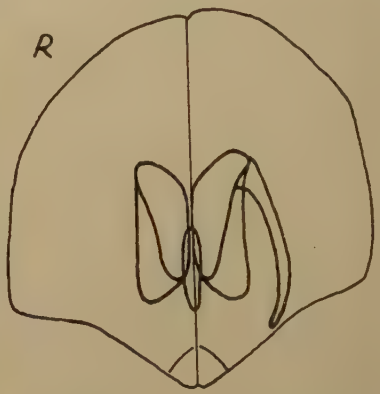


FIG. 398.—SEMI-AXIAL SAGITTAL ANTERO-POSTERIOR VENTRICULOGRAM SHOWING SYMMETRICAL LATERAL VENTRICLES, MIDLINE THIRD VENTRICLE AND COMPLETELY FILLED LEFT TEMPORAL HORN.

The right temporal horn can be filled at will by appropriate manipulation of the head.

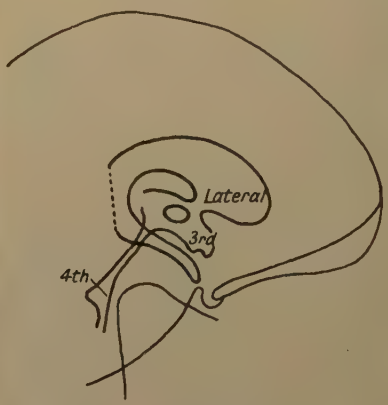


FIG. 399.—LATERAL SUPINE ENCEPHALOGRAM (BROW UP) SHOWING FILLING OF THE WHOLE SYSTEM.

under local anæsthesia and is usually well tolerated at the age of five years in girls and seven years in boys. Below these ages general anæsthesia must be induced.

Through a short scalp incision made in the post-parietal regions on each side, burrholes are made in the skull, the dura opened in cruciform manner and special brain needles inserted directly into the lateral ventricles. All cerebro-spinal fluid obtained is replaced by air and the periosteum, galea and skin closed with interrupted black silk sutures.

This method should always be made use of when papillœdema or a raised intracranial pressure is present, and in all cases of cranio-cerebral injury where an expanding lesion is suspected. Grave complications, including sudden death, may follow attempts at cisternal or lumbar encephalography in cases with high intracranial pressure.

Radiographic technique.—This is the same by whichever route air has been injected, the aim being to obtain pictures of all parts of the ventricular and subarachnoid systems by manipulation of the head in appropriate positions. The air will always travel to the uppermost part of the cerebro-spinal fluid spaces, displacing such fluid as may remain and may thus be induced to fill any part of the system at will. Full details may hardly be given here but the main principles are to take three views with the patient supine: (1) an antero-posterior, (2) semi-axial sagittal antero-posterior, and (3) lateral: these will outline the anterior half of the ventricular system and subarachnoid space. The patient is next turned into the prone position and three similar views obtained: postero-anterior, semi-axial sagittal postero-anterior and lateral, when the posterior part of the systems fill. Finally one or more lateral views may be taken with the head on one side. Further and more complicated manœuvres are required to fill the aqueduct of Sylvius and the fourth ventricle, when antero-posterior and lateral views with the patient prone, are then taken.

From observation of the accompanying series of X-ray films (fig. 397–404) of normal ventricular systems it will be seen that the lateral ventricles, apart from the occipital horns which are occasionally asymmetrical, are almost exactly similar in size, shape and position. Normal lateral ventricles vary considerably in size and shape from one individual to another. In lateral views the foramen of Monro, by which the lateral ventricles communicate with the third ventricle, can easily be seen. The third ventricle should always be exactly in the midline in antero-posterior and postero-anterior views, extending downward and forward to its optic and infundibular recesses which lie above the sella turcica. In the centre of the third ventricle is a clear oval area which does not fill with air and is produced by the middle commissure (or massa intermedia) running across the cavity of the ventricle. The posterior part of the third ventricle extends upwards and backwards into the suprapineal and infrapineal recesses whilst postero-inferiorly it is continuous with the Sylvian aqueduct which curves backwards and downwards into the posterior fossa. The aqueduct and fourth ventricle also lie exactly in the midline in antero-posterior and postero-anterior views. The aqueduct

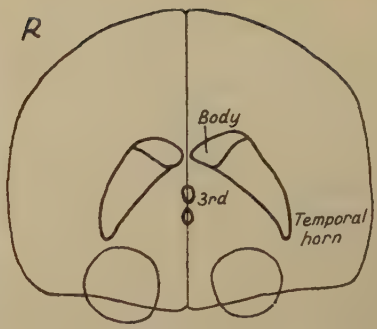
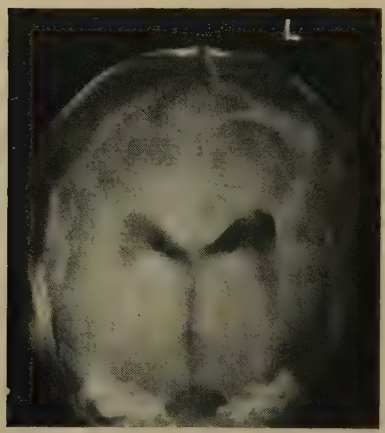


FIG. 400.—POSTERO-ANTERIOR ENCEPHALOGRAM SHOWING SYMMETRICALLY SITUATED LATERAL VENTRICLES WITH SOME AIR IN THE MIDLINE THIRD VENTRICLE.



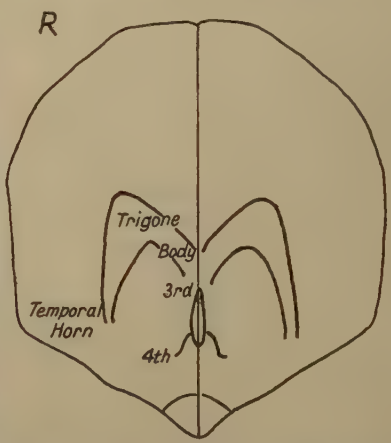


FIG. 401.—SEMI-AXIAL SAGITTAL POSTERO-ANTERIOR VENTRICULOGRAM SHOWING POSTERIOR PART OF BODY, TRIGONE AND TEMPORAL HORN OF EACH LATERAL VENTRICLE.

Some air is present in the third and fourth ventricles.

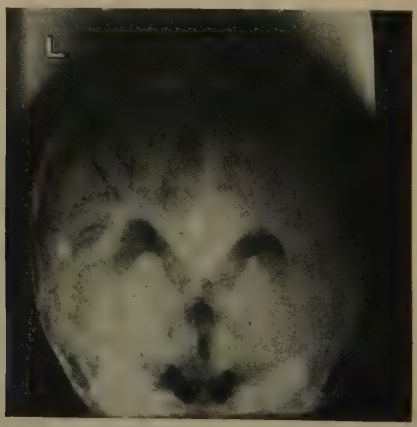


FIG. 402.—IDENTICAL VIEW IN AN ENCEPHALOGRAM SHOWING NORMAL CONVOLUTIONAL MARKINGS AND AIR IN SUBARACHNOID SPACE.

opens out at its lower end into the fourth ventricle which appears as a tent-like or triangular shadow in lateral views, lying in the anterior part of the cerebellar fossa.

When air has been introduced by cisternal or lumbar puncture a picture of the subarachnoid space and basal cistern is also obtained in the majority of cases.

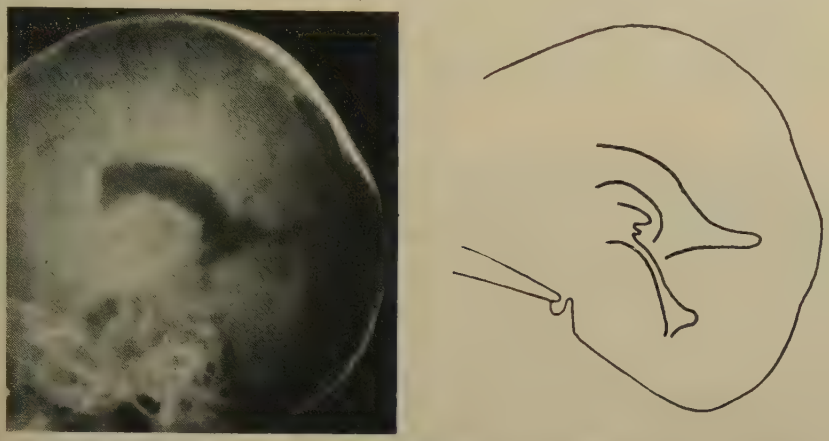


FIG. 403.—LATERAL PRONE ENCEPHALOGRAM SHOWING NORMAL BODY, TRIGONE AND OCCIPITAL HORNS.

The posterior part of the third ventricle is seen with its supra- and infra-pineal recesses. The aqueduct and fourth ventricle are also seen.

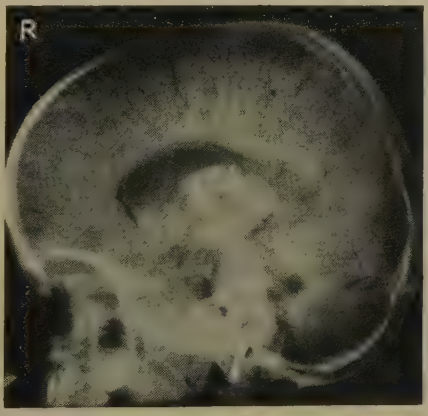


FIG. 404.—FULL LATERAL ENCEPHALOGRAM SHOWING WELL-FILLED VENTRICULAR SYSTEM AND NORMAL CONVOLUTIONAL MARKINGS OVER THE HEMISPHERES.

Tumour of the cerebral hemispheres.—The ventriculographic appearances give a most accurate guide to the real localization and size of such lesions. The system is shifted as a whole to the opposite side whilst the forward, backward and downward shift of the lateral ventricle of the affected side gives more precise information still. It is safe to say

that the ventriculographic appearances enable the surgeon to expose the whole lesion in 95 per cent. of cases so that radical extirpation of the growth (if this is possible) may be achieved.

Suprasellar tumours.—In the majority of such cases the initial straight skiagrams will have disclosed definite evidence in the form of calcification (fig. 405) either within or above the sella turcica, erosion of the clinoid processes, expansion of the sella and widening of the sutures of the vault with enlargement of the vault as a whole. Such information, however, does not disclose the total extent of the tumour which must be assessed by air studies. As the tumour expands it first compresses the anterior end of the third ventricle, then occludes the foramina of

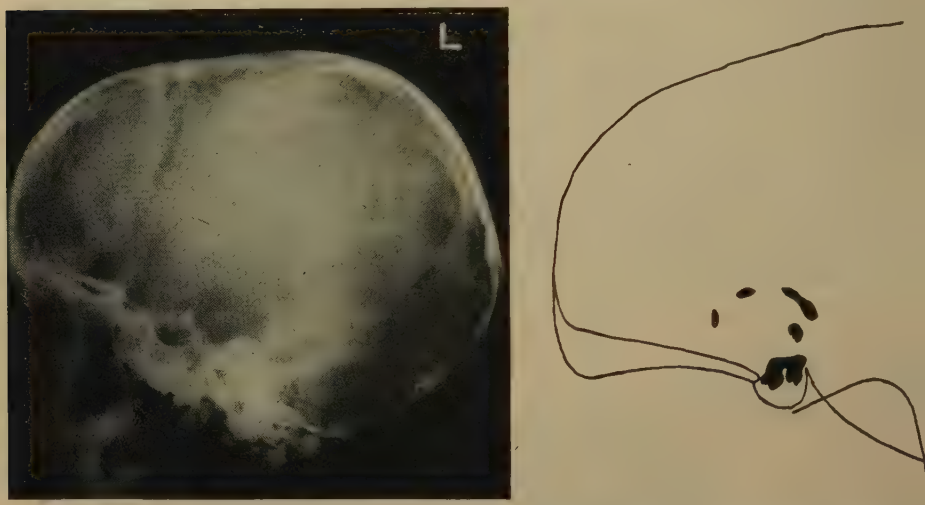


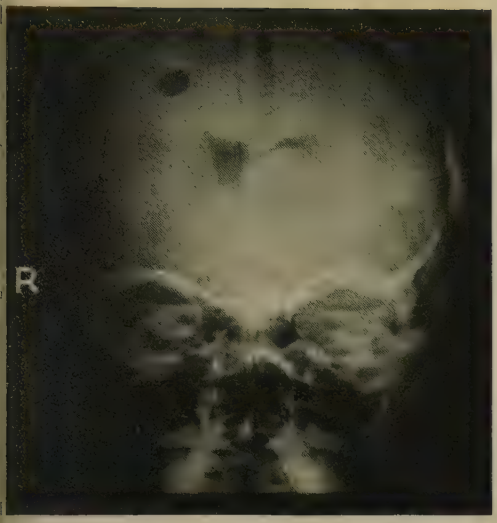
FIG. 405.—STRAIGHT LATERAL X-RAY PICTURE FROM A CASE OF CRANIOPHARYNGIOMA SHOWING POSITION OF SUPRASELLAR CALCIFICATION.

Monro with resultant dilatation of the lateral ventricles, finally producing a filling defect on the under surface of one or both lateral ventricles (fig. 406, 407).

Tumours of basal ganglia.—Such lesions lie extremely close to the ventricular system producing only localized, but little, if any, general displacement. Ventricular air studies give extremely accurate localization of such tumours (fig. 408-411).

Intraventricular tumours.—The majority of tumours within the ventricular system (in children) are invasive gliomata, and by reason of their histological characteristics and position are irremovable. Their localization, however, is easily established.

Unilateral dilatation will occur if one foramen of Monro be obstructed, or, bilateral dilatation if both are occluded. Filling defects of the third ventricle are associated with tumours arising from the roof, walls or choroid plexus of the ventricle.



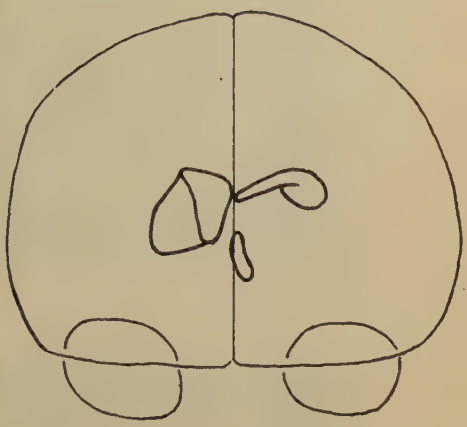


FIG. 406. ANTERO-POSTERIOR VENTRICULOGRAM FROM THE SAME CASE (AS FIG. 405) SHOWING MARKED UPWARD DISPLACEMENT OF ANTERIOR HORN OF LEFT LATERAL VENTRICLE AS WELL AS SOME UPWARD DISPLACEMENT OF THIRD VENTRICLE.

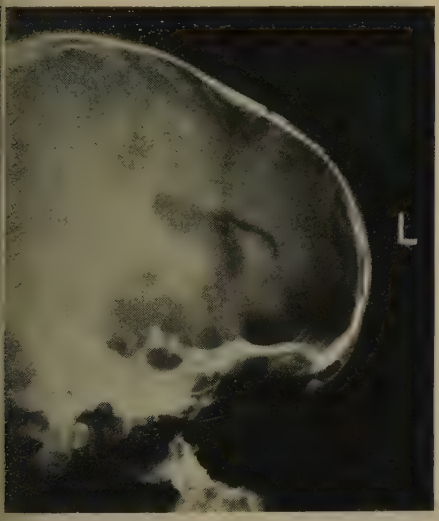


FIG. 407.—LATERAL SUPINE VENTRICULOGRAM SHOWING CALCIFICATION AND UPWARD DISPLACEMENT OF LEFT ANTERIOR HORN, REVEALING THAT THE TUMOUR IS CONSIDERABLY LARGER AND HAS SOME EXTENSION FORWARDS INTO THE FRONTAL LOBE.

At operation a large extension of the tumour forwards into the frontal lobe was confirmed. The additional evidence produced by air study is well exemplified in this case.

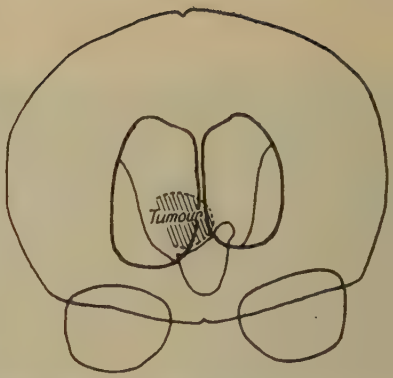
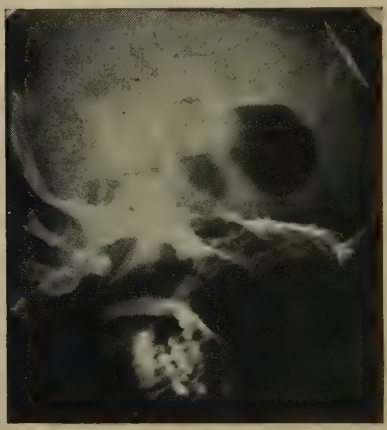


FIG. 408.—ANTERO-POSTERIOR VENTRICULOGRAM SHOWING DILATATION OF THE LATERAL VENTRICLE AND THE ANTERIOR PART OF THE THIRD VENTRICLE.

A filling defect in the left lateral aspect of the third ventricle is also visible.



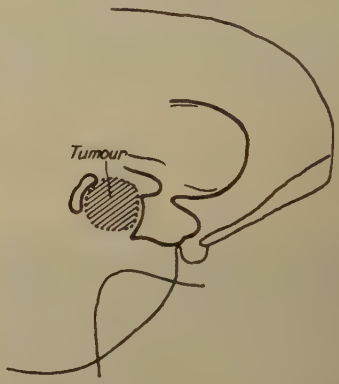


FIG. 409.—LATERAL SUPINE VENTRICULOGRAM SHOWING DILATED LATERAL VENTRICLE, ENLARGED FORAMEN OF MONRO AND ANTERIOR HALF OF THIRD VENTRICLE.

Some air has been manipulated past the tumour to outline its posterior extremity. A case of tumour arising in the optic thalamus extending into the third ventricle and producing partial obstruction.

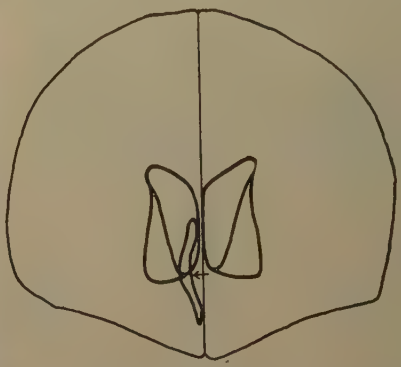
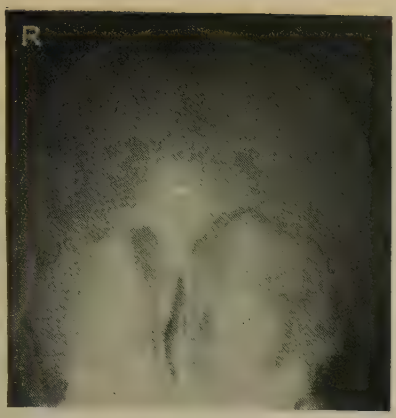


FIG. 410.—ANTERO-POSTERIOR VENTRICULOGRAM SHOWING DISPLACEMENT OF CENTRAL PORTION OF THIRD VENTRICLE TOWARDS THE RIGHT.

No obstruction to the cerebro-spinal fluid pathway has yet taken place.



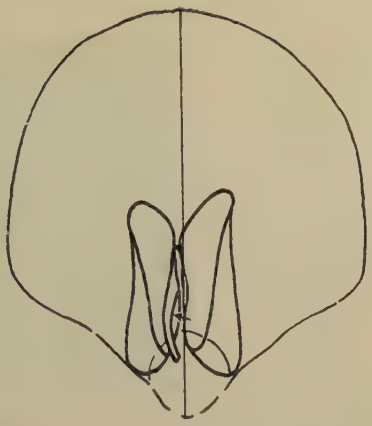
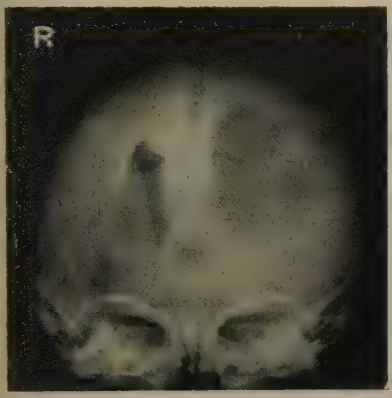


Fig. 411.—Semi-axial Sagittal Antero-posterior Ventriculogram to show Filling Defect in greater Detail.

From the localized deformity the tumour must be close to the ventricle in the basal ganglia and be inaccessible to surgery.



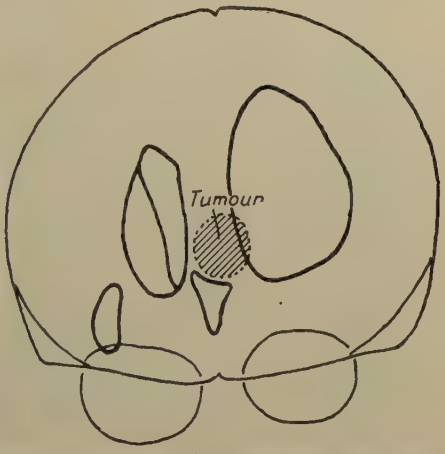
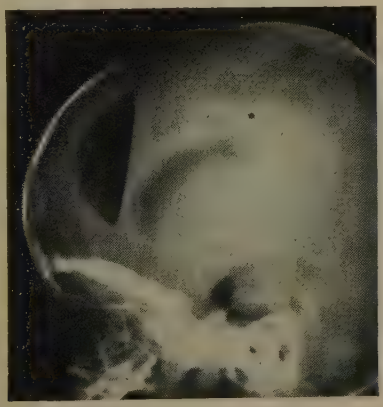


Fig. 412.—Antero-posterior Ventriculogram showing Dilatation of the Left Lateral Ventricle, shift of the Right Lateral Ventricle towards the Right Side and a Filling Defect in the Upper Part of the Third Ventricle.



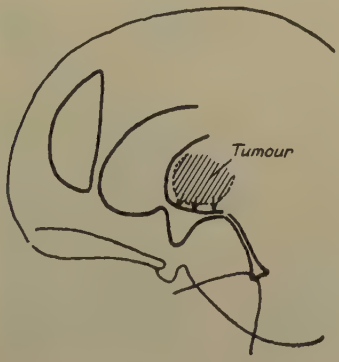


Fig. 413.—Lateral Supine Ventriculogram showing Filling Defect in Upper Part of Third Ventricle, presumably from a Tumour arising in its Roof.

A malignant glioma in this situation was confirmed by transventricular operation.

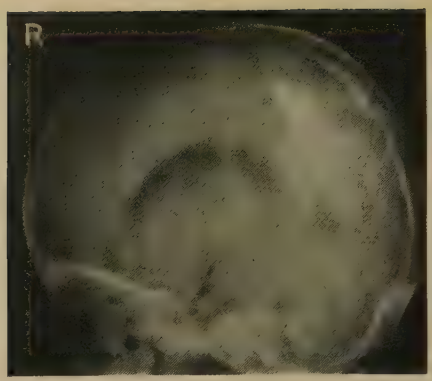
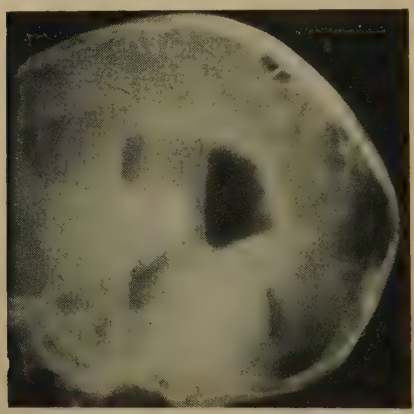


FIG. 414.—LATERAL SUPINE VENTRICULOGRAM SHOWING DILATATION OF LATERAL VENTRICLE (THE RIGHT CONTAINING LITTLE AIR), GREAT BROADENING OF THE LEFT FORAMEN OF MONRO AND COMPLETE ABSENCE OF FILLING OF THE THIRD VENTRICLE.

The appearances are those of a large tumour filling the third ventricle and this was confirmed at operation.



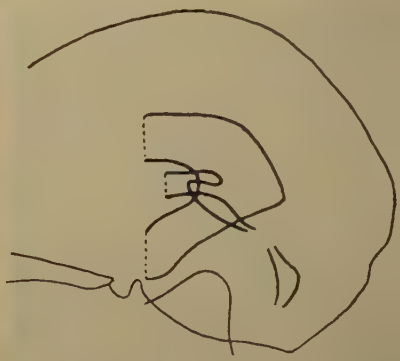
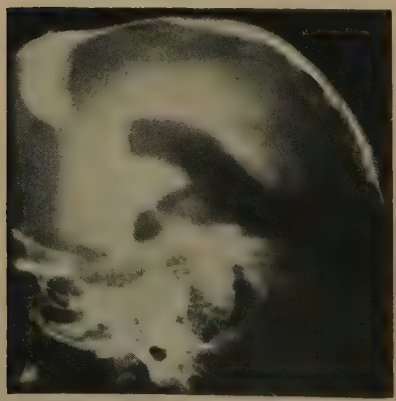


FIG. 415.—LATERAL PRONE VENTRICULOGRAM SHOWING ELONGATION AND BACKWARD DISPLACEMENT OF THE AQUEDUCT OF SYLVIUS AND FOURTH VENTRICLE INDICATING A TUMOUR LYING ANTERIORLY IN THE PONS.



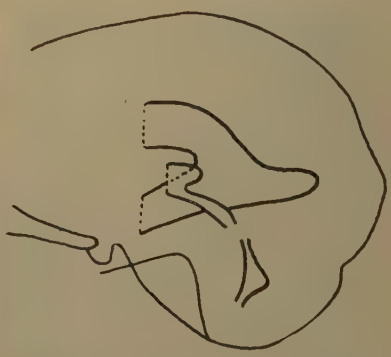
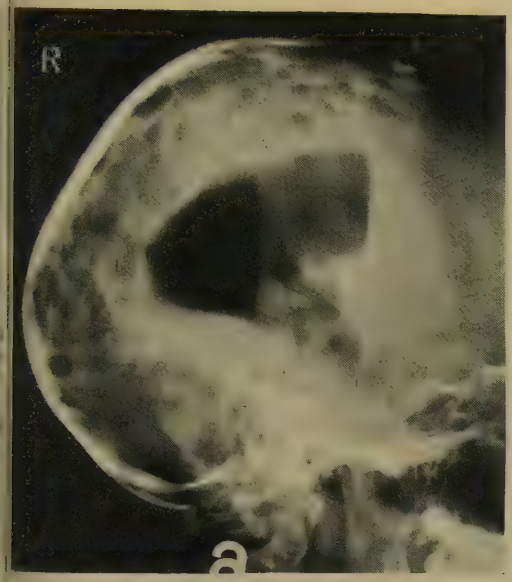


FIG. 416.—LATERAL PRONE VENTRICULOGRAM SHOWING SIMILAR APPEARANCE BUT MARKED DISPLACEMENT.

Again from a case of proven pontine tumour.



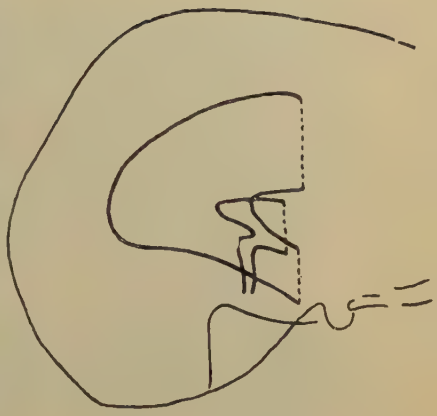
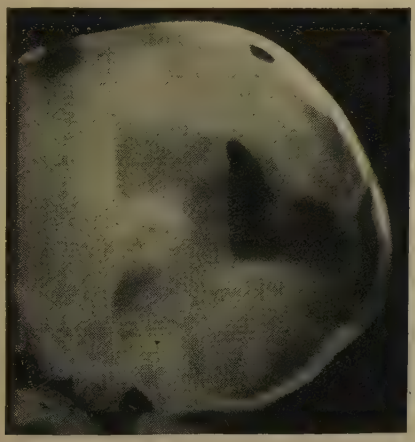


Fig. 417. -Lateral Prone Ventriculogram showing Dilated Lateral Ventricles and Forward Displacement of the Aqueduct with Kinking of its Supratentorial Portion.

The appearances are those of a large supra-fastigial vermis tumour and were confirmed at subsequent operation.



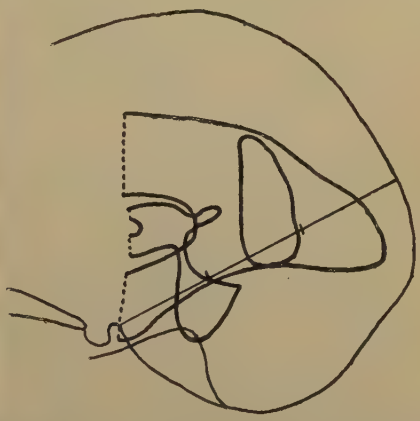


Fig. 418.—Lateral Prone Ventriculogram showing Dilatation of Lateral Ventricles, Forward Displacement of the Aqueduct and upward shift of the Fourth Ventricle.

Similarly tumours of the pineal region will show expansion of both lateral ventricles and of the anterior portion of the third ventricle with a filling defect of the posterior part of that ventricle (fig. 412–414).

Mid-brain tumours. As the aqueduct and fourth ventricle lie in the midline, axial views will indicate a shift to one or other side giving lateralization of the lesion. The normal aqueduct of Sylvius in lateral views curves downwards and backwards crossing the junction of the middle and inner thirds of a line drawn from the posterior clinoid processes to the lambdoidal suture. Forward or backward displacement can be estimated in this manner.

If the Sylvian aqueduct is obstructed a symmetrical hydrocephalus results and only that part of the aqueduct above the lesion will fill with

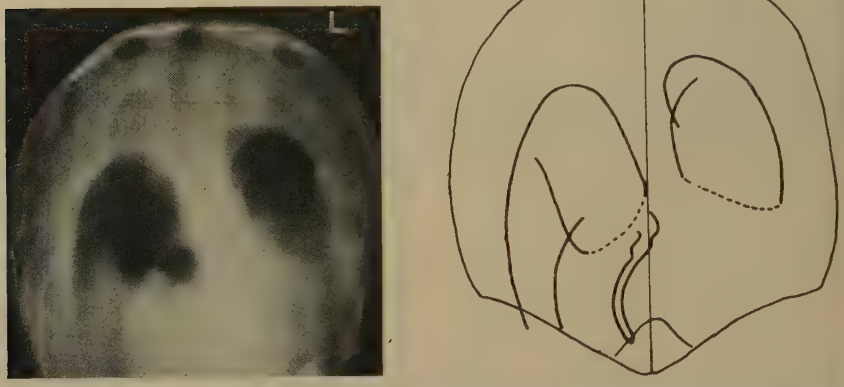


FIG. 419.—SEMI-AXIAL SAGITTAL POSTERO-ANTERIOR VENTRICULOGRAM SHOWING GROSS DILATATION OF LATERAL VENTRICLES AND SHIFT OF AQUEDUCT AND FOURTH VENTRICLE TO THE RIGHT SIDE.

From these two skiagrams the tumour should lie mainly in the left cerebral hemisphere below the fastigium. This proved to be the case at subsequent operation.

air. Other growths will produce forward, backward or lateral displacement of the aqueduct according to their primary situation, but complete occlusion usually results eventually (fig. 415, 416).

Subtentorial tumours.—Tumours arising in the upper part of the vermis (above the fastigium) produce first a forward displacement of the aqueduct with kinking of its upper portion and later almost complete aqueduct obstruction. Tumours lying in one or other hemisphere will shift the ventricular system to the opposite side whilst infra-fastigial vermis tumours displace the fourth ventricle forwards and upwards.

Tumours lying within the fourth ventricle show an appropriate filling defect in the air shadows of this cavity.

Non-space-occupying lesions.—Much aid may be obtained from air studies of the ventricular and subarachnoid systems when investigating children presenting as cases of mental deficiency, epilepsy or congenital abnormality of the central nervous system.

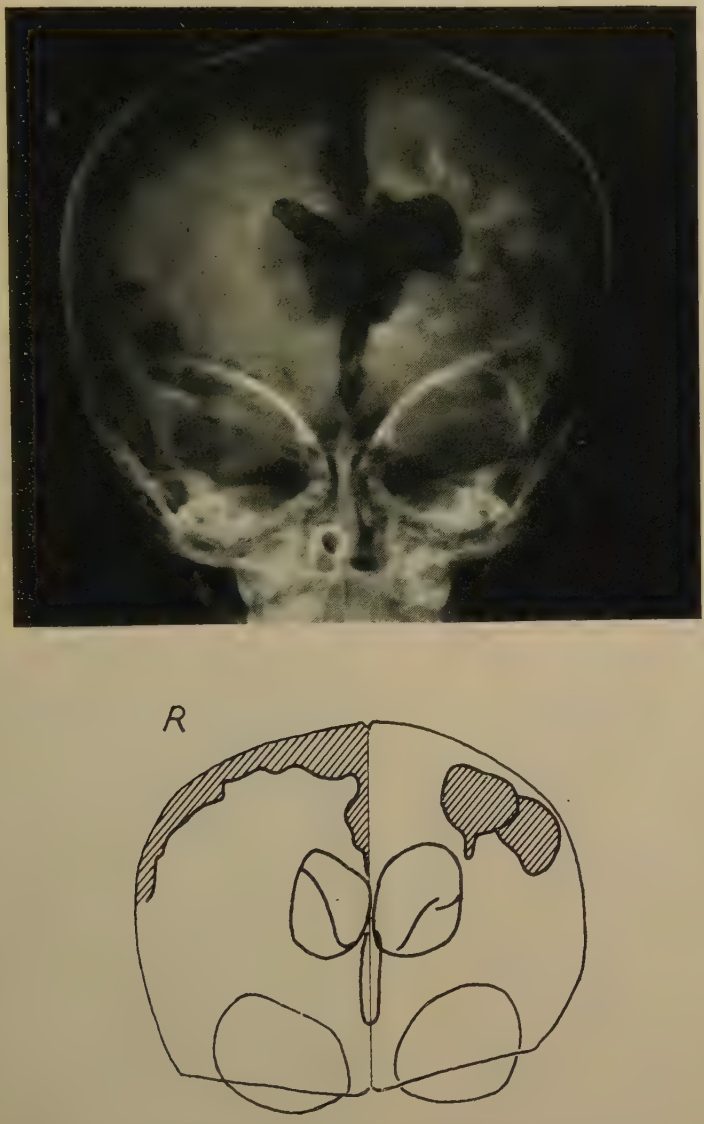


Fig. 420.—Antero-posterior Encephalogram showing Slight Enlargement of Left Lateral Ventricle, large Collections of Air over the Left Hemisphere and great Increase in Depth of Subarachnoid Space over the Right Hemisphere.

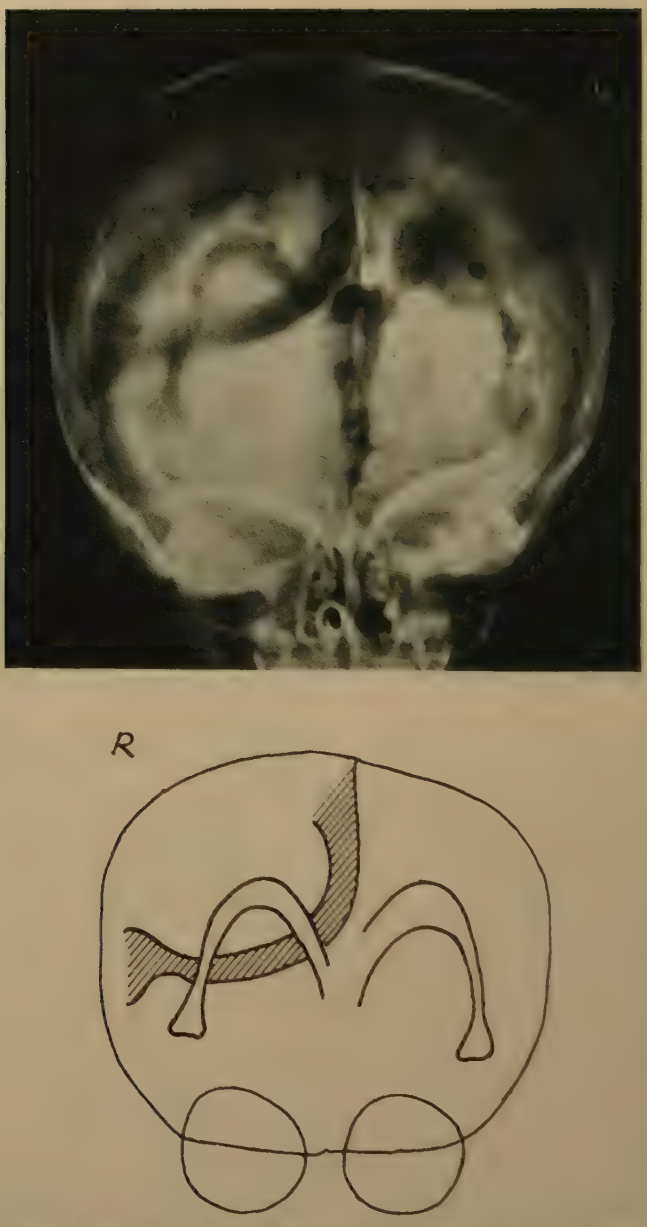
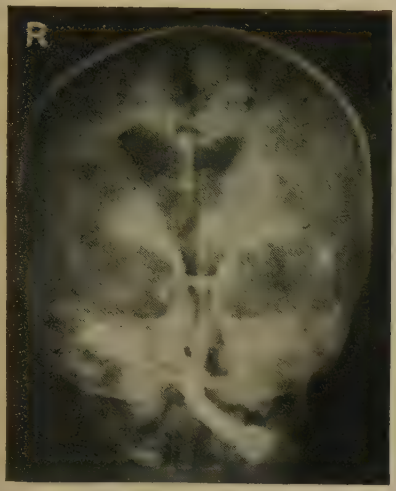


FIG. 421.—SEMI-AXIAL SAGITTAL POSTERO-ANTERIOR ENCEPHALOGRAM SHOWING LARGE SUBARACHNOID SPACE ON RIGHT SIDE LYING BETWEEN THE HEMISPHERE ON THE ONE HAND AND THE FALX AND TENTORIUM ON THE OTHER.

This indicates considerable shrinkage of the hemisphere on that side.

In patients with *congenital hemiplegia*, for example, it is common to find dilatation of the lateral ventricle of the appropriate cerebral hemisphere



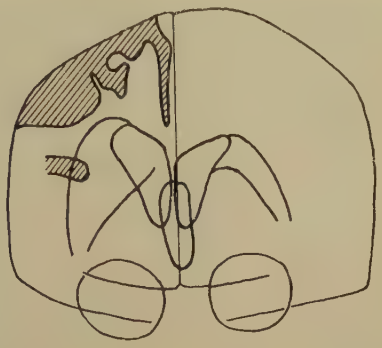
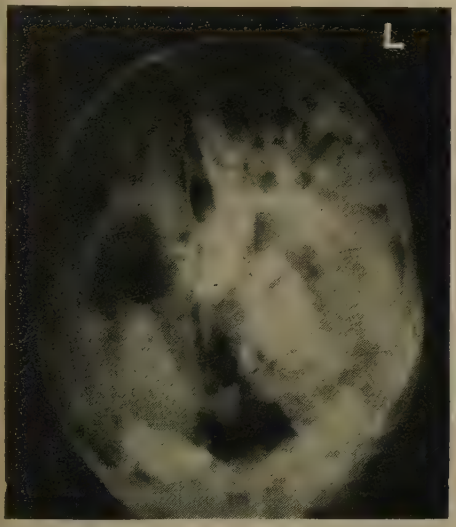


FIG. 422.—ANTERO-POSTERIOR ENCEPHALOGRAM SHOWING RIGHT HEMIATROPHY OF THE SKULL, DILATATION OF THE ENTIRE RIGHT LATERAL VENTRICLE AND GROSS ATROPHY OF THE RIGHT CEREBRAL HEMISPHERE INDICATED BY THE VERY DEEP AIR-FILLED SUBARACHNOID SPACE AND LARGE AIR SPACE ALONGSIDE THE FALX.



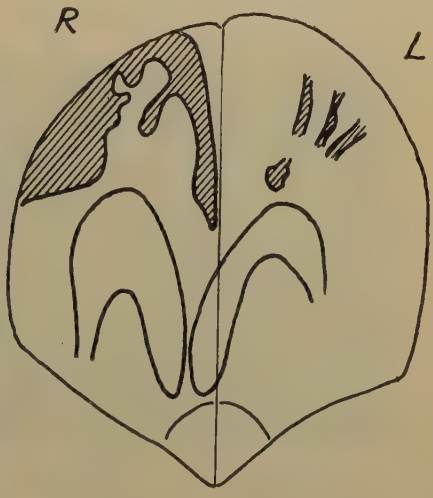


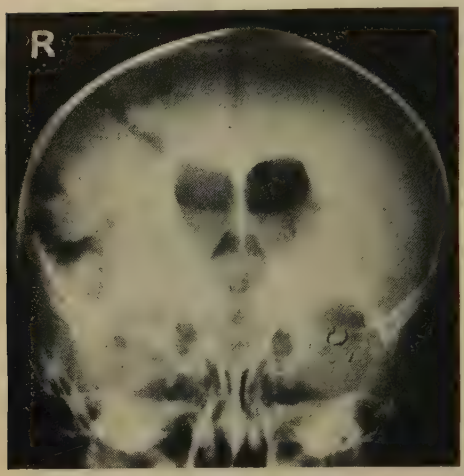
FIG. 423.—SEMI-AXIAL SAGITTAL ANTERO-POSTERIOR ENCEPHALOGRAM OF THE SAME CASE SHOWING, IN ADDITION, ENLARGED SULCI IN THE LEFT HEMISPHERE.

associated with increase in size of the cortical air shadows indicating an agenesis or atrophy of the hemisphere (fig. 420, 421).

Many cases of *epilepsy* and *mental defect* are found to have lesser or

greater degrees of *atrophy* or *agenesis* of one or both cerebral hemispheres (fig. 422–425).

Porencephalic cavities in the brain are often revealed in unexplained



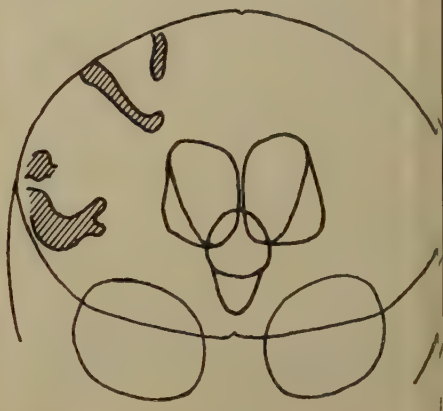
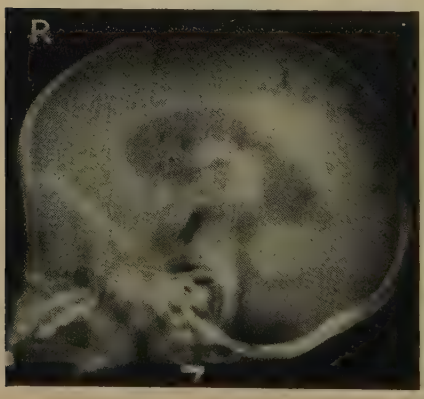


FIG. 424.—ANTERO-POSTERIOR ENCEPHALOGRAM SHOWING SYMMETRICAL ENLARGEMENT OF LATERAL VENTRICLES, GROSS EXPANSION OF THE THIRD VENTRICLE AND GREATLY ENLARGED CORTICAL SHADOWS IN THE RIGHT HEMISPHERE.

The large ventricular system indicates a diffuse cerebral atropy or agenesis and the big cortical shadows confirm this.



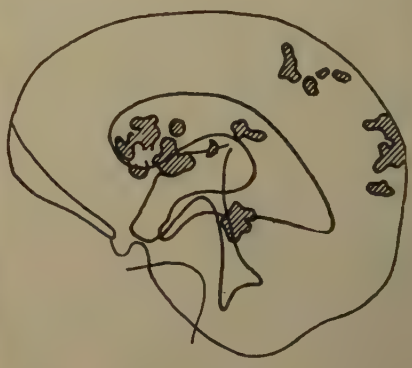


FIG. 425.—LATERAL ENCEPHALOGRAM SHOWING DILATATION OF THE ENTIRE VENTRICULAR SYSTEM AND GREAT PUDDLES OF AIR LYING IN THE SUBARACHNOID SPACE INDICATING SHRIVELLED CEREBRAL CONVOLUTIONS.

cases of local or generalized epileptiform convulsions and in cases of monoplegia or hemiplegia. The revelation of such gross organic changes as those mentioned above is of great significance and of considerable help in assessing the prognosis (fig. 426–428).

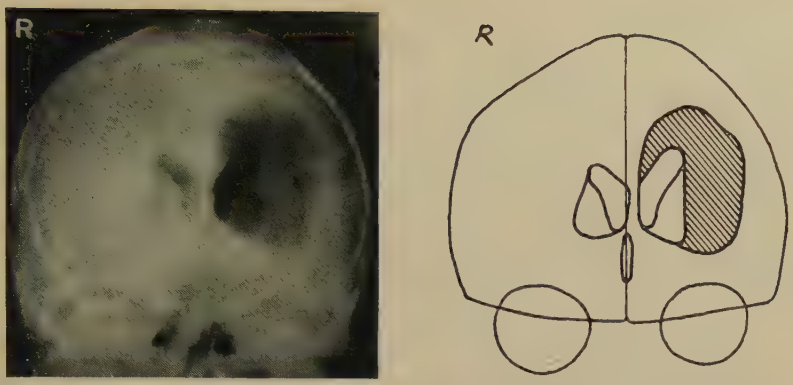


Fig. 426.—Antero-posterior Encephalogram showing large Porencephalic Cavity and slight shift of Ventricular System towards the Side of the Lesion.

There is also asymmetry of the skull, the affected left side being smaller than the right.

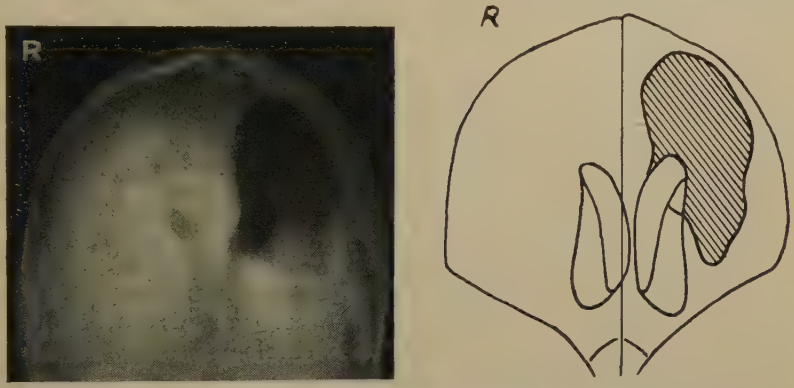


Fig. 427.—Semi-axial Sagittal Antero-posterior Encephalogram showing large Porencephalic Cavity and slight shift of Ventricular System towards affected Left Side.

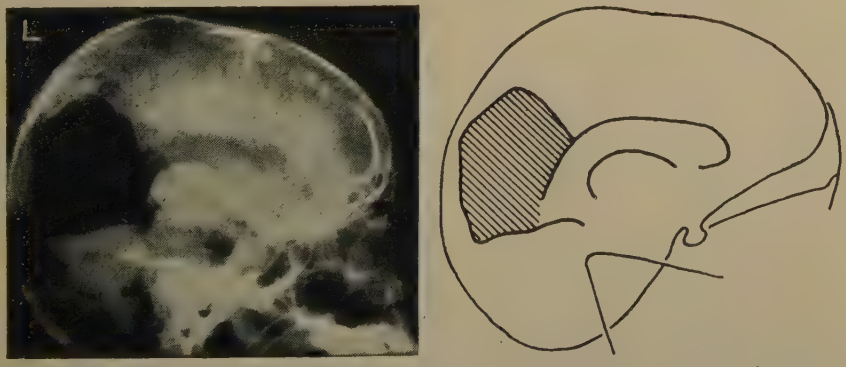


Fig. 428.—Lateral Encephalogram showing Large Left Parieto-Occipital Porencephaly.

VIRUS AND OTHER FORMS OF ENCEPHALO-MYELITIS

Within the last quarter of a century the recognized forms of encephalitis have notably increased. The distinction of individual types seldom depends upon symptomatology, but is reached more often through animal experiment, immunology, bacteriology, and pathology. To simplify description they can be divided into four groups.

(1) Encephalitis of virus causation.

(2) Encephalitis of unproved ætiology, but characterized pathologically by demyelination of nerve fibres.

(3) " Incidental " encephalitis where the brain lesions are not an essential part of the disease, but similar to those occurring in other parts of the body.

(4) Toxoplasmosis causing encephalo-myelitis.

(1) **Virus encephalitis.**—A *neurotropic* virus has an affinity for ganglion cells of the grey matter within which it becomes fixed. From its point of entry, nasopharynx, gut, or wound, it passes to the neuraxis along axonal pathways. The viruses of polio-myelitis and of rabies are examples of the neurotropic type. That of mumps is potentially neurotropic, and may give rise to meningo-encephalo-myelitic symptoms. Rarely, during infection with a *viscerotropic* virus, as in glandular fever (Bernstein, 1940), in infective hepatitis (Newman, 1942), in " atypical pneumonia " (Hein, 1943), nervous complications have occurred probably by a blood transmission of antigen.

Certain viruses appear peculiar to man, notably those of poliomyelitis, epidemic encephalitis and herpes zoster. Others normally pathogenic for animals can be transferred to man by direct transmission, as in rabies, swineherd's disease, acute lymphocytic choriomeningitis. An indirect transmission by an insect intermediary is a possibility, the mosquito in equine encephalitis in both its forms eastern and western (Feemster and Getting, 1941).

In many of the virus diseases a characteristic feature of the lesions in the nervous system is the presence within degenerating ganglion cells and glial cells of a specific intranuclear change, referred to as an *inclusion body*. A few cases in children with many similarities of symptomatology and pathology, a subacute encephalitis with clonic and dystonic movements of the limbs, ataxy, spasticity, coma, a normal cerebro-spinal fluid, and *post mortem* the presence of inclusion bodies in nerve and glial cells of the Rolandic cortex, basal ganglia and anterior and posterior horns of the spinal cord have been referred to as " inclusion encephalitis " (Dawson, 1934 ; Akelaitis, 1942 ; Brain, Greenfield and Russell, 1943).

(A) POLIOMYELITIS (see p. 1299).

(B) EPIDEMIC ENCEPHALITIS, Type A encephalitis (see p. 1308).

(C) EPIDEMIC ENCEPHALITIS, Type B of Japan ; the St. Louis type ; Equine encephalitis ; and Australian X disease. The Japanese type of encephalitis is due to a filterable virus, immunologically distinct from other forms, and has occurred in repeated epidemics. The other types

mentioned appear to be virus infections of animals with occasional transference to man, in some instances by an insect vector. No cases of these types have been recognized in this country.

Encephalitis type B and the St. Louis type of 1933 have affected adults mainly. Equine encephalitis, both the eastern and western forms (Webster and Wright, 1938), and Australian X disease have had a high incidence and heavy mortality among infants and children. In them the symptoms have been those of any acute encephalitis, with excess of lymphocytes in the spinal fluid, and in the pathology, vascular engorgement, perivascular cuffing, cellular infiltration, areas of necrosis and nerve cell degeneration in the cortex, basal ganglion, pons and medulla and spinal cord.

(D) Meningo-encephalo-myelitis in association with herpes. In herpes zoster there are inflammatory changes of the sensory or dorsal root ganglia and in the corresponding areas of skin. Sometimes a pleocytosis of the cerebro-spinal fluid is indicative of a meningeal irritation. In ophthalmic zoster especially, symptoms of a meningo-encephalitic type have occurred, and post-mortem perivascular lymphocytic infiltration witnessed in the thalamus, hypothalamus, cerebellar nuclei and medulla. Most cases of meningo-encephalitis complicating zoster have been in elderly people (Biggart and Fisher, 1938). The close relationship between zoster and chickenpox and the occurrence of a meningo-encephalitis with either condition suggests that a common virus is responsible. An attack of zoster appears to give a lasting immunity. The virus has not yet been transmitted to animals.

The virus of herpes simplex as an agent in the production of an encephalitis has been suspected, but its ubiquity shown by its skin lesions in so many febrile patients and as a chance finding in the spinal fluid or brain, without previous signs of encephalitis, or of herpetic eruptions, has made the possibility seem a remote one. The virus is a specific filterable one and has been found in the saliva, tears, and has also been proved to be the cause of aphthous stomatitis occurring in infants and young children (Burnet and Williams, 1939), at which age, therefore, its involvement of the central nervous system would seem most likely. Smith, Lennette and Reames (1941) report a fatal case of acute encephalitis in an infant of four weeks, in which a virus recovered from the cerebral tissues was identified as that of herpes simplex and intranuclear inclusion bodies similar to those seen in proved herpetic lesions were found in degenerating nerve cells. The following case supports the view that the virus of herpes simplex is capable of producing central lesions in the nervous system.

A boy of seven and a half years since the age of four years had in combination, or separately, two attacks of left facial paralysis with incomplete recovery, and three attacks of right oculomotor paralysis, one attack of right facial paralysis, and finally paralysis affecting the triceps, carpi radialis, indicis and communis digitorum of the left arm without recovery and with loss of excitability to faradism in three months. Except in the first attack, a crop of herpetic vesicles always appeared on the right side of the chin, usually a few days after onset of the cranial nerve palsies, but preceding the paralysis

on one occasion. The paralysis was ushered in with headache, and swelling of half the face and severe pain behind the ear with the facial paralyses. The child had other herpetic outbreaks on the chin when he had a cold or catarrh. The Wassermann was negative and the cerebro-spinal fluid normal (Wyllie, 1932).

FIG. 429.—RIGHT INTERNAL RECTUS AND LEFT FACIAL PALSIES IN ASSOCIATION WITH HERPES SIMPLEX (SEE TEXT).
(By courtesy of Editors, *Proc. roy. Soc. Med.*)

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(2) **Acute disseminated encephalo-myelitis,** spontaneous and complicating the specific fevers and vaccination (anatomically, acute perivascular myelinoclasis). This is a heterogeneous group with a fairly uniform symptomatology of meningeal irritation of sudden onset, seldom insidious, with rapid development of cerebral and spinal paralyses. The cases are mostly sporadic, but small epidemics without obvious contact

between cases have occurred, and children and young adults are chiefly affected.

Ætiology.—The agents productive of the myelinoclastic reaction are unknown. Theories favour the presence of a latent neurotropic virus activated spontaneously, or by an acute exanthem, or contend that the primary virus of the exanthem, or its toxins, are responsible. Other views suppose degenerative, deficiency, and allergic or sensitization causes.

Pathology.—The characteristic feature is of patches, often sharply delimited, of demyelination around and along the small blood vessels, chiefly in the white matter of the cerebral hemispheres, cerebellum, brain-stem, and spinal cord. A moderate perivascular cellular infiltration and sometimes petechial hæmorrhages are also observed (Turnbull and McIntosh, 1926; Greenfield, 1929).

Symptomatology.—In the cases which complicate the infectious fevers, the nervous symptoms commonly begin four to seven days after the primary rash which is in a state of decline and the patient afebrile, and there appears to be no connection between the occurrence of nervous symptoms and the severity of the primary exanthem. In a few cases the nervous symptoms have occurred with the rash, or as late as three weeks afterwards.

Meningeal symptoms of sudden onset are headache, fever, vomiting, nuchal rigidity, pains in the limbs, and convulsions. Cerebral symptoms rapidly appear, giddiness, delirium and drowsiness which often deepens into coma. Other signs are diplegia, hemiplegia, tonic rigidity, tremor and choreiform movements, ataxy, aphasia, dysarthria and dysphagia. Of cranial nerve paralyses, facial weakness is commonest, ocular palsies rarely occur, but trismus is frequently seen, and has suggested a diagnosis of tetanus. A slight degree of swelling of the discs is frequently present. Myelitic signs are those of a transverse myelitis with sensory disturbances and retention of urine, which is a common symptom and may persist for several days, or more simply an abolition of the tendon reflexes. A characteristic feature of many cases is a state of coma with statuesque rigidity of the trunk and limbs, the legs extended, the face immobile, which may last for a few days up to two or three months. A sudden increase or reduction in the severity of the symptoms is common. In a personally observed case of post-vaccinal encephalitis coming on eleven days after a primary vaccination in a girl of ten years, examination on the third day of nervous symptoms discovered a state of coma, and statuesque rigidity with absent knee- and ankle-jerks, extensor plantars and incontinence. Six hours later the patient was conscious, able to ask questions rationally, the tendon reflexes were present and the plantar responses flexor.

The duration of symptoms is usually one to several weeks, and the mortality has been highest in the post-measles and vaccinal cases. In non-fatal cases recovery is often complete, but permanent sequelæ are common in those complicating measles.

The cerebro-spinal fluid in this group of encephalopathies shows a

slight rise of proteins, and a small or moderate increase of cells, usually monocytes, but is often normal. A progressive diminution of chlorides and glucose does not occur, which, along with the sudden onset, helps to distinguish these cases from tuberculous meningitis.

Treatment.—Lumbar puncture helps to relieve the meningeal symptoms. The use of appropriate convalescent human sera has been advocated, but its value is doubtful, as viruses take up an intracellular station, and, moreover, it is uncertain that the nervous complication can be attributed directly to the virus of the primary exanthem.

Post-vaccinal encephalo-myelitis has occurred for the most part after primary vaccination, but in a few instances has followed revaccination. Infants under six months are least often affected, but cases have occurred in sucklings of a few weeks to a few months of age. In England and Wales from 1922 to 1927 there were ninety-three cases, of which nine were in infants under one year. Rolleston stated the proportion of cases with nervous sequels was one of every 33,000 vaccinations, and of deaths, one to every 66,000 vaccinations. More recently, of half a million people vaccinated in Glasgow (1942), Anderson and McKenzie reported an incidence of seven cases of post-vaccinal encephalitis (one to 71,000), of which two died, and six were primary vaccinations in persons over five years of age. In Fife (1942) eight cases of vaccinal encephalitis occurred in a group of 53,772 recently vaccinated persons (one in 6,600) with a case mortality of 44 per cent. (Fyfe and Fleming, 1943). A mortality between 30 and 40 per cent. has been fairly constantly observed. Fyfe and Fleming consider that human immune serum given early in large doses, 140 c.cm. intramuscularly and intravenously, is of value, which would suggest that the virus of vaccinia is the causal agent.

Smallpox encephalo-myelitis.—In the period 1928–31, out of 40,313 cases of smallpox in England and Wales, for the most part mild infections, Marsden and Hurst (1932) recorded ten cases with an encephalo-myelitic syndrome. With one exception the ages were below fifteen years.

The measles form began to be more prevalent in 1924 and is now the type most frequently seen. Residual defects are common, such as hemiplegia, diplegia, speech disturbance and abnormal behaviour. Ford (1938) placed the rate of recovery at 25 per cent., death 10 per cent., and sequelæ 65 per cent. Not all forms of measles encephalitis are of the myelinoclastic type. In some cases with onset of nervous symptoms with or even preceding the rash the lesions suggest an acute toxic or hæmorrhagic encephalitis.

The chickenpox form.—Up to 1936 about 120 cases of nervous complications following varicella were recorded by Underwood (1938). Cerebellar and myelitic signs were the commonest, the cerebellar syndrome being ataxy, vomiting, giddiness, tremor, nystagmus and blurred speech. Dagnelie and van Bogaert in sixty-nine cases found four were fatal, about 80 per cent. recovered completely, and slight or severe sequelæ persisted in 13 per cent.

The German measles form is the least common and the nervous symptoms may be cerebral, cerebellar, or spinal. In 1937, Read found

records of eighteen cases with ages of three to thirty-three years. Demyelination has been found in one case, and perivascular lymphocytic cuffing and œdema in another.

The spontaneous form of acute encephalo-myelitis has a similar symptomatology to that already described, and in a few fatal cases demyelination has been present (Redlich, 1927). The incidence has been chiefly in young adults.

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(3) **Incidental or acute toxic encephalo-myelitis** serves to describe a group of cases of varied pathogenesis but of similar symptomatology, mostly affecting young children, and usually of sporadic occurrence, though sometimes in small epidemics. It covers those cases in children of mixed meningo-encephalitic and myelitic syndromes complicating some bacterial infection arising elsewhere in the body. The following have been complicated by acute toxic encephalitis: scarlet fever, erysipelas, streptococcal pharyngeal and otitic infections, measles, and broncho-pneumonia. Nervous symptoms may precede the rash, or occur at its height in scarlet fever and measles, depending on the degree of toxæmia. Small epidemics of unknown causation have been reported by Brown and Symmers, ten fatal cases of " acute serous encephalitis " in children of from two to seven years of age ; by Braithwaite and Innes as " epidemic serous meningitis " in thirteen children from nine weeks to six years of age, of which five cases were primary and six secondary to broncho-pneumonia ; and by Brain and Hunter as acute meningo-encephalo-myelitis of childhood in a series of cases between three and eighteen years of age.

Pathology.—The characteristic lesions consist of congestion, focal collections of glial cells, perivascular œdema, proliferation of vascular endothelium, and ganglion cell degeneration. Sometimes hyperæmic extravasations of red cells are seen neighbouring the vessels (acute hæmorrhagic encephalitis). Grinker and Stone (1928) relate these changes to a toxicosis, or reaction to bacterial toxins, rather than to a result of microbic invasion. A subgroup, probably of toxic origin, described as acute hæmorrhagic leuco-encephalitis by Weston Hurst (1941), shows a hæmorrhagic inflammation concentrated mostly in the central white substance of the hemispheres and characterized clinically by a rapidly fatal course with hemiplegia, coma, pyrexia and a leucocytosis. The spinal fluid is usually normal.

Symptomatology.—The nervous symptoms are of sudden onset and resemble those of a purulent meningitis. In severe cases signs of cerebral and spinal involvement are hemiplegia, monoplegia, or diplegia,

urinary retention, and absence of deep reflexes with extensor plantars. The spinal fluid is under pressure, clear, may contain a fibrin clot, and has normal percentages of chlorides, glucose, and a normal cell count or moderate increase of lymphocytes. The mortality in the small epidemics has been variable, but recovery is often complete.

In the nervous complications of *whooping-cough*, the pathology is varied. An acute degeneration of ganglion cells with little or no vascular or glial tissue reaction has been described by Husler and Spatz (1924). The clinical syndrome of pertussis eclampsia usually commences about the third week of whooping when the paroxysmal bouts are diminishing, and consists of multiple convulsions and coma, leaving hemiplegia, diplegia, mental impairment and blindness, and is often fatal.

Cerebral symptoms in *scarlet fever* may be due to encephalitis, uræmia, and to vascular lesions embolic or thrombotic usually giving rise to a permanent hemiplegia.

In *typhoid*, nervous symptoms, hemiplegia, aphasia, athetosis, or spinal symptoms, may be due to thrombotic lesions, or to toxic degeneration of nerve cells (Thewalt, 1928). During epidemics of *influenza*, cases of encephalitis and polyneuritis have occurred, and either acute hæmorrhagic lesions or perivascular demyelination found in the central nervous system (Greenfield, 1930). Toxic encephalopathies due to the *diphtheria* toxin reaching higher neurons are rare, but choreo-athetosis as a sequel has been described. More frequently hemiplegia and athetosis complicating diphtheria are of embolic origin from clotting in the auricles in cases with cardiac weakness. Rolleston observed six cases of hemiplegia in 9,075 cases of diphtheria.

Encephalopathies of the "toxic" type, besides being caused by bacterial toxins, can be produced by a variety of organic and inorganic substances, for example, lead encephalopathy (see p. 1318), sulphanilamide encephalopathy with lesions of a demyelinating type (Fisher and Gilmour, 1939), and demyelination following arsphenamine therapy and carbon monoxide poisoning (Hurst, 1941).

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(4) **Protozoal encephalitis ; toxoplasmosis.**—Toxoplasma, a genus of protozoon, is capable of becoming an intracellular parasite in man, though more commonly found in animals and birds. The method of human infection is unknown, but the parasite is distributed by the blood stream, causing lesions in lung, liver, kidney, muscles, or brain.

The first definite case in Great Britain appears to have been described by Jacoby and Sagorin in 1948. Since then several other cases have been reported, and it may be that the disease is more common than was formerly thought.

The infantile type originates *in utero*, often from an inapparent maternal infection, giving rise to a state of hydrocephalus or microcephaly, retinochoroiditis, encephalomyelitis and intracerebral calcification. Convulsions in the neonatal period or later are common. Retinochoroiditis with macular changes and scattered yellow-white patches and areas of black pigmentation are of diagnostic importance. The spinal fluid has been described as xanthochromic with a lymphocyte increase, but nothing pathognomonic of the disease has yet been reported. Sabin (1941) described the disease as an acquired infection in two children aged six and eight years with signs of a non-suppurative encephalitis, one being fatal while the other made a good recovery. The symptoms were headache, vomiting, convulsions, weakness, but neck rigidity and fever were absent. The fundi in both cases were normal. We have knowledge of three similar cases in this country.

The diagnosis is confirmed by recovering the toxoplasma from animals inoculated with blood, cerebro-spinal fluid or other tissue from a suspected case, and by demonstrating toxoplasma antibodies in the infected serum. Neutralizing, complement-fixing and cytoplasm-modifying antibodies have been described by Sabin and Ruchman (1942), Warren and Russ (1948) and Sabin and Feldman (1948) respectively. In addition, toxoplasma antigen has been used as a skin test. The titres of diagnostic significance in these various tests are not yet firmly established, but in cases where the clinical findings are suggestive of toxoplasmosis it is usual to obtain some correlation between the three serum antibodies. What reliance can be placed on the skin test is uncertain, as in America Feldman and Sabin (1949) have found 65 per cent. of the population over the age of forty years to be toxoplasmin-positive.

The development of the disease in mice seems to be retarded by penicillin, some sulphonamides and aureomycin, but there is little evidence that these drugs can modify the disease in man. With aureomycin, indeed, we have caused what appeared to be an acute exacerbation of meningo-encephalitis.

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POLIOMYELITIS

Synonyms.—Acute infantile paralysis, Heine-Medin's disease, Epidemic paralysis.

Introduction.—Infantile paralysis was made notifiable in 1912 under the title of "acute poliomyelitis and polioencephalitis." In a clinical

sense, the second half of the title is unfortunate as it has lent itself to the indiscriminate labelling of so many obscure cases of acute hemiplegia in children as polioencephalitis. Whereas on the side of morbid anatomy, its use is strictly accurate, because of the constancy of cerebral as well as of spinal lesions in fatal human cases, yet in these same cases there is an absence of clinically recognizable cerebral paralysis, if temporary disturbances of cerebral function in the acute febrile stage, and cranial nerve palsies, which brain-stem lesions are closely analogous to those of the spinal cord, be excluded. In most cases of permanent cerebral paralysis a clinical diagnosis of polioencephalitis is erroneous.

Poliomyelitis occurs either sporadically or in epidemics. The first epidemic to be recorded was in Sweden in 1881, and the countries which have suffered most from epidemic visitations have been America, Australia, Norway and Sweden. Sporadic cases occur at any period of the year, but the seasonal incidence in the northern hemisphere is greatest in late summer and early autumn, while March and April are the months of prevalence in the southern hemisphere.

The disease tends to affect children between the ages of one to three years more than at any other period of life. Children less than six months old are rarely affected, though cases have been recorded in the first few weeks of life. The sexes are equally susceptible. An average mortality of 12 to 14 per cent. has been recorded for various epidemics.

Ætiology.—The method whereby the human becomes infected remains unsolved, but the manner of spread and the pathways utilized by the infective agent within the nervous system are being revealed by research.

The infective agent is accepted to be a minute filter-passing micro-organism anærobically culturable, which was first identified by Flexner and Noguchi in 1913. In 1909, Landsteiner and Popper, using inoculating material from the brain and spinal cord of a fatal human case, had succeeded in reproducing the disease in monkeys. By natural means of infection the virus affects man only. In artificially inoculated animals different species have their separate types of response, which, if taken as prototypes of the human disease, are often misleading.

Portals of entry in the human body.—The pharynx and intestine appear to be the common sites of entry. In man, the presence of the virus has been found in nasopharyngeal washings and in the fæces of active and convalescent cases, as well as abortive cases and contacts. From the same sources it has been found in fatal cases, and in addition recovered from the nasopharyngeal mucosa, tonsil, walls of the small and large intestine, and mesenteric lymph-nodes. The presence of the virus in human fæces was first demonstrated in 1912 by Kling, Pettersson and Wernstedt. The readiness with which it can be found in the fæces of the paralysed and their close contacts suggests the intestinal wall as a site of its propagation, but there is as yet no evidence to show whether its habitat is intestinal epithelium, lymph nodes, or intestinal nerve ganglia.

The virus can also be readily recovered from the oral pharynx. In

districts with a recurring epidemicity, the tonsillar pharynx appears to be a frequent portal, judged by the number of cases recognized to have followed tonsillectomy during the epidemic season. Aycock has collected a total of 2,857 such cases. Abrasions of the skin may possibly provide portals of entry, as cases of poliomyelitis have occurred after wading, paddling, or swimming in virus-contaminated water.

The persistence of virus in different sites shows great variation.

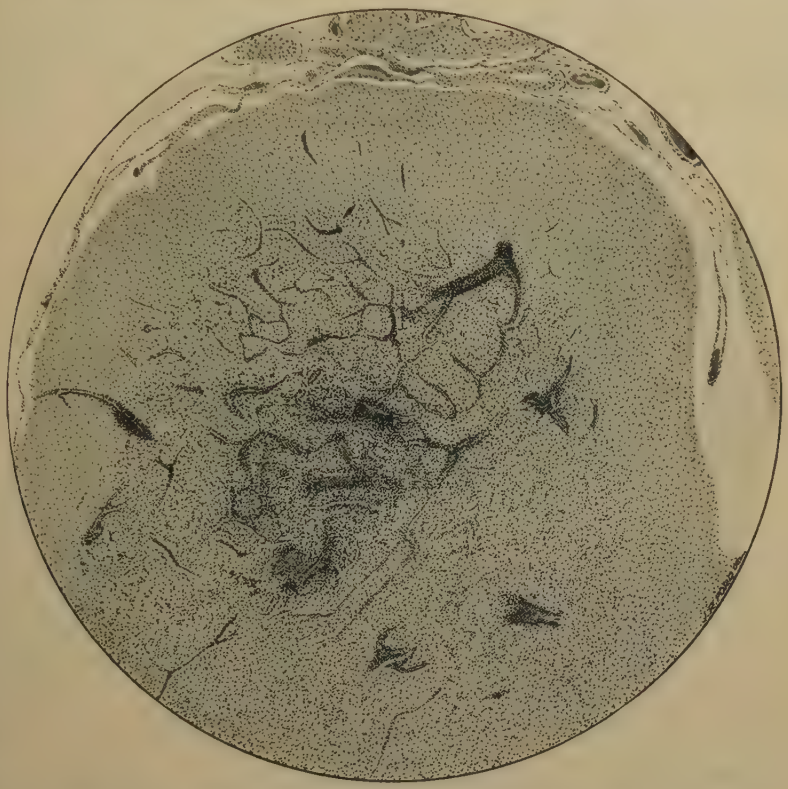

FIG. 430.—SECTION OF THE SPINAL CORD FROM A CASE OF ACUTE POLIOMYELITIS OF ONE MONTH'S DURATION, SHOWING ENGORGEMENT AND PERIVASCULAR LYMPHOCYTOSIS AFFECTING CHIEFLY THE VESSELS OF THE GREY MATTER OF THE ANTERIOR HORN, BUT AFFECTING ALSO THE WHITE MATTER AND, TO A SLIGHT EXTENT, THE MEMBRANES.

From the nasopharynx it was not found after the fifth day of the disease, but was present in the stools of convalescents for as long as four months. Carriers include convalescents, abortive cases and contacts.

VIRUS OUTSIDE THE HUMAN BODY.—Trask and Paul have proved its presence in sewage during urban epidemics. Therefore contaminated waterways may be a natural source of virus. A gastro-intestinal entry is supported by a theory of water transmission. In contaminated milk the survival of virus has been estimated at thirty-one days. Dissemination

of virus by insects is possible, as it has been demonstrated in the bodies of several species of flies in epidemic areas.

Pathways to the central nervous system.—Early theories of transmission were based upon the experimental disease in rhesus monkeys, which are now known to be resistent to any form of "natural" infection by polio virus except by nasal inoculation and so through the olfactory bulbs. Using higher apes more likely to be analogous to man in their response, Howe and Bodian infected chimpanzees orally with virus-containing fæces and the spread of lesions could be traced to cranial nerve nuclei; but olfactory lesions were absent. In fatal human cases, Sabin and Ward failed to find the virus in the olfactory mucosa. Inoculating chimpanzees by the gastro-intestinal route through a stomach-

Fig. 431.—Section of the Spinal Cord from a Case of Poliomyelitis of Three Months' Standing, showing Softening and Destruction of the Whole of the Grey Matter of the Anterior Horns.

The section has been stained by the Marchi method, and the fatty products of degeneration are stained black. The child had complete flaccid paralysis of the lower extremities.

tube, Howe and Bodian found lesions in the cœliac ganglia, sympathetic chains of ganglia, and in the spinal cord.

In man, access to the nervous system is neither by the blood nor by the cerebro-spinal fluid, as both are devoid of virus during the disease.

Pathways within the nervous system.—Fairbrother and Hurst claimed that the spread of virus proceeded along axones and not by perineural lymphatics. The axones themselves are unaffected, but damage occurs at the ganglion-cell stations. The greater severity of lesions of the spinal cord than of the brain in human cases may be said to favour either a spinal entry from the gut, or a selective preference of the virus for spinal ganglia. Virus can travel from brain to spinal cord, or vice versa, and in both directions from a bulbar invasion and by motor or sensory nuerons, sympathetic or vagal. The rate of transmission as estimated by Bodian and Howe using neurons of peripheral nerves of rhesus monkeys was 5 to 8 cm. a day.

Cerebral and spinal lesions in human poliomyelitis.—Both in

man and monkey the virus shows a "system selectivity" within the central nervous system. The most susceptible areas are the grey matter of the spinal cord, the cranial nerve nuclei, the precentral motor cortex, hypothalamus, vestibular and associated nuclei. Cerebral lesions are diffuse and lack the saturation of spinal lesions, and thus fail to give rise to signs clinically detectable except temporary or preparalytic symptoms of a diffuse or general nature. Howe and Bodian refer to the "neglected encephalitis which accompanies the spectacular myelitis." In the experimental animal, instances of lesions in the cord without any being present in the brain were not observed, but an encephalitis could occur unaccompanied by any pathological change in the cord in abortive cases.

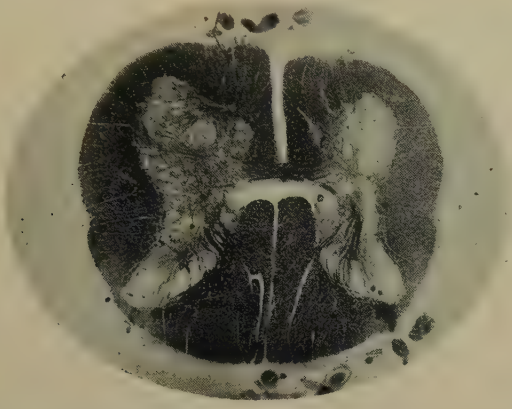

FIG. 432.—SECTION OF THE SPINAL CORD OF A CHILD WHO, TWO YEARS BEFORE DEATH, HAD SUFFERED FROM POLIOMYELITIS, GIVING RISE TO FLACCID PARALYSIS OF ONE LEG.

The grey matter of the cord on the affected side is greatly atrophied, and contains but few nerve cells. Stained by Weigert-Pal method.

The virus causes damage or destruction on entering ganglion cells, and in the acute stage the local condition is aggravated by vascular engorgement and œdema. Histological findings are neuronophagia, vascular cuffing, focal infiltrations and glial reaction.

Symptomatology.—There are three modes of onset in the paralytic cases. First there is the "morning paralysis" of Charles West, occurring in less than a quarter of the sporadic cases. The child not observed to be ailing awakes in the morning with a paralysed limb. The other two types both start with symptoms of an acute febrile illness. In one, the commoner, there is a progression without interruption to the paralytic stage, whereas in the other a period of remission after three or four days' illness is followed by an aggravation of the febrile disturbance culminating in the paralysis—the dromedary type of fever of Draper.

After known exposure to infection in epidemics, the preparalytic symptoms appear within six to eighteen days. Common initial symptoms are fever 100–103° F., headache, and pains in the back and muscles of

the limbs. Sore throat, vomiting, diarrhœa or constipation, often occur as early symptoms in epidemics especially, and are suggestive of an "influenzal" or a gastro-intestinal infection, possibly food-poisoning. There is, however, little evidence of a primary systemic infection in man or animal, as in the chimpanzee or rhesus monkey inoculated intra-cerebrally, prodromal symptoms, fever, lethargy, prostration, tremor, appearing after one or several days, precede the appearance of paralysis of the limb by a further variable period.

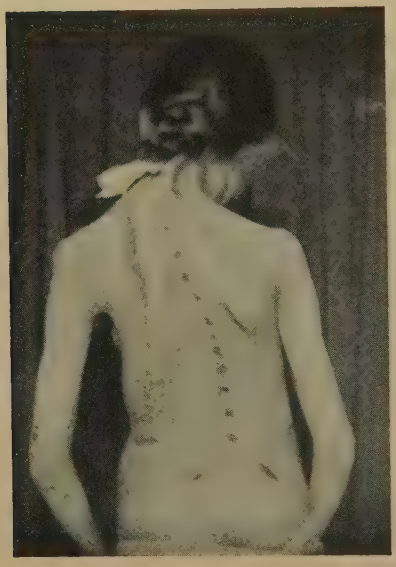

FIG. 433.—CURVATURE OF THE SPINE AFTER POLIOMYELITIS.

FIG. 434.—POLIOMYELITIS AFFECTING THE SHOULDER AND UPPER ARM MUSCLES ON BOTH SIDES.

Note wasting of shoulder and upper arm muscles.

The more definite signs of meningeal and cerebral disturbance occurring early or later in cases of sudden or gradual onset, or in the second phase of the dromedary type of febrile reaction, are neck-stiffness, drowsiness to stupor combined with irritability, clumsiness due to ataxy, tremor or twitching, convulsions occasionally in younger children, and early exaggeration of the tendon reflexes. Signs of brain-stem involvement are nystagmus, facial palsy, hoarseness or aphonia, difficulty in swallowing, and irregularity of the pulse or tachycardia. It is inaccurate to state that the paralysis in all cases is at its height at the moment of its appearance. Careful inquiry will make it clear that the paralysis often spreads over contiguous muscles—ascending and descending forms

—or can appear elsewhere at a distance the jump type—over a period of several days before the fever departs.

Severe spinal and muscle pains, pre- and post-paralytic, depend on increased fluid tension in the theca and infiltrative cellular lesions along the sensory nerve roots and in the posterior root ganglia. Hyperæsthesia, a common symptom, is similarly to be accounted for.

The cerebro-spinal fluid in the preparalytic stage sometimes contains a high proportion of polymorphs, but usually lymphocytes are in excess at all stages. During the first week of paralysis a pleocytosis of fifty to one or two hundred cells is common, with a rapid fall to a nearly normal figure by the end of the second week. The protein content, by contrast, is at first almost normal, but rises to a maximum in about the third week, from 0·03 gm. up to about 0·2 gm. per 100 c.cm.

Various forms of paralysis are described. The spinal is the commonest, and the lumbar enlargement is more often involved than the cervical. The characteristic flaccid paralysis is followed by wasting of the affected muscles, and there is abolition of tendon reflexes in the affected segments. The muscles of the leg below the knee are the most commonly affected and the anterior tibial group seem specially liable to be involved. Urinary retention for twenty-four hours or so is a common initial symptom along with paralysis of the legs when the lumbo-sacral ganglia are involved. In some cases at an early stage the plantar response may be extensor, when the inflammatory process in the grey matter of the cord has overflowed into the more laterally situated pyramidal tract.

Fig. 435.—Poliomyelitis giving rise to Left Facial Paralysis.

The child had, in addition to the above, paralysis of the neck and shoulder muscles on the right side, and her brother was simultaneously affected with the same disease.

When the cervical region of the cord is involved, it is much more often the muscles of the shoulder-girdle than those of the forearm and hand which are affected. A paralysis of the small muscles of the hand is usually only found in association with a complete flaccid paralysis of a whole arm. Paralysis of a single muscle, such as a winged scapula due to weakness of the serratus magnus, is sometimes caused by a local lesion in the lower cervical region of the cord. The cervical sympathetic may be paralysed with narrowing of the palpebral fissure and smallness of the pupil.

When the thoracic segments of the cord are involved, paralysis of the abdominal and intercostal muscles results, and respiration may be carried on solely by means of the diaphragm and accessory muscles. Paralysis

of the dorsal muscles of the back is liable to give rise to curvature of the spine.

In the bulbo-pontine or brain-stem form, an extensive involvement of the medulla is rapidly fatal from paralysis of vital centres. This form seldom occurs separately. Paralysis of cranial nerves is often observed at an early stage of any form of poliomyelitis, but normally disappears completely. Ruhräh and Mayer noted affection of the cranial nerves in forty-six out of 338 cases of poliomyelitis, with individual nerve involvement in the following proportion : facial, 26 ; sixth nerve, 12 ; oculomotor, 2 ; glossopharyngeal, 2 ; optic, 2 ; fourth nerve, 1 ; hypoglossal, 1.

Meningitic and abortive forms are recognizable in epidemics. In them, presumably, the virus has made its encephalitic invasion but has been arrested before myelitic lesions have occurred.

Immunity : second attacks.—An attack of poliomyelitis almost always affords immunity against reinfection. Rare instances of a second attack have been recorded. Still, in 1930, on reporting such a case, found records in the literature of eight others. The interval between first and second attacks has been from two to fifteen years.

Diagnosis.—In infants, poliomyelitis has to be differentiated from the pseudo-paralyses of scurvy and syphilis. An Erb's brachial palsy may be confused with poliomyelitis unless a natal history with presence of paralysis at birth is obtained. Tuberculous caries of the spine with disinclination to walk, or a psoas abscess with pain, loss of power in one leg and an absent knee-jerk, may suggest a poliomyelitis.

Recent research suggests that some cases of so-called *non-paralytic poliomyelitis* are due to Coxsackie viruses 1 or 2, first isolated in the village of that name in New York State. These viruses are associated with Bornholm disease, or epidemic myalgia, in which a meningeal lymphocytic reaction may occur. There is reason to believe that these viruses are also widely distributed in Great Britain (Findlay).

Treatment.—Serum therapy.– Human convalescent serum possesses neutralizing power. If injected with, or immediately after antigen, the experimental animal can be protected, but once the virus becomes active in the central nervous system, serum is ineffective. In the preparalytic stage of the human disease the virus is already within the ganglion cells, beyond the influence of circulating antibody. The conclusion reached by the U.S.A. International Committee for the Study of Infantile Paralysis, 1932, was that there was no indication that convalescent serum either procured a reduction in case mortality or prevented paralysis.

Passive immunization of child contacts with 10 c.cm. or more of pooled adult sera intramuscularly has yet to be proved of value.

The paralyses.—A paralysed muscle in a state of stretch from the unopposed pull of healthy muscles is doubly weak, and a most thorough examination of the state of all muscle groups is essential. From the onset of paralysis optimum physiological rest of affected muscles is attained by placing them in a position of relaxation with the aid of pillows, sandbags and improvised splints. Movements passive and active should not be begun until muscular tenderness has disappeared, usually within a period

of three weeks. Patients with respiratory difficulty will require to be placed in a respirator.

The severity and extent of the paralysis often shrinks within a few days of the onset, as the œdema and vascular inflammation within the affected segments of the spinal cord subsides. Permanent paralysis is restricted to those muscles whose cellular representatives in the anterior horn cells have been destroyed, whereas complete or partial recovery occurs in those muscles whose ganglionic connections in the cord have only suffered temporary eclipse or partial damage. Muscles which show no signs of returning function within a period of six months are beyond hope of improvement. The presence of a good reaction to faradism in a paralysed muscle is a sign that recovery will occur. Treatment of paralysed muscles includes many forms of physiotherapy, massage, active and passive movements short of tiring, diathermy and exercise in water. It must be clearly understood that their value is limited to sustaining a healthy circulation and nutrition of affected muscles, pending such time as is needed for the repair of nerve cells that have escaped total destruction and for the regeneration of their neurons. Improvement can be hoped for under suitable therapy up to two or three years. As soon as possible the ambulant stage should be reached by means of adequate splints of a type readily removable for purposes of massage and hydrotherapy. Enclosing a limb in plaster conceals the state of the muscles and prevents many useful forms of physiotherapy from being used.

FIG. 436.—CHILD WEARING CELLULOID SPLINTS IN WALKING APPARATUS.

The child had flaccid paralysis of both legs below the hips due to poliomyelitis.

In cases of severe paralysis, a limb will lag behind its opposite in growth, and arthrodesis and other orthopædic measures may be required to bring the limb back into use. As a rare event following an attack of poliomyelitis, progressive muscular atrophy may supervene at a later age in the muscles afflicted by the earlier disease.

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ENCEPHALITIS TYPE A

(or Epidemica, or Lethargica)

This is considered to be due to a neurotrophic virus with an affinity for ganglion cells within which it becomes fixed, reaching the central nervous system from the nasopharynx. The virus appears to occur "naturally" in man only, either sporadically or in epidemics. Although not a new disease, since 1916 when von Economo described it as encephalitis lethargica, its prevalence temporarily became notably increased and it appeared in all parts of the globe. In England and Wales it was made notifiable in 1919 and the heaviest epidemic incidence was in the years 1921–3–4 and 5. Subsequently it has declined to a few sporadic cases yearly presenting only the symptoms of the chronic stage, while the acute stage once so common has almost disappeared. Distinctive features of encephalitis type A are ocular paralyses, Parkinsonism, and behaviour changes.

Ætiology.—The disease appears to be transmitted by healthy carriers. Instances of case to case infection in households are uncommon, but suggest that the disease is to a slight degree contagious. Its prevalence has been greatest in the cold season of the year, winter and early spring. The period of incubation is unsettled. The age-period most affected has been that between the tenth and thirtieth years, but infancy is not immune. From 1919 to 1925 Shrubsall stated that of 1,325 verified cases notified in London, 338 were under sixteen years of age. The disease is not self-limited, and the virus is capable of lying dormant to smoulder again even after an interval of eight years. In childhood a larger number of males have been affected. The average death-rate in epidemics was about 40 per cent.; complete recovery in roughly 25 per cent.; and some residual defect in the remainder.

Pathology.—Macroscopically, the brain may show no abnormality, but a pink congested appearance and possibly petechial hæmorrhages are common, and the grey matter on cut surfaces may be "plum-coloured." Any part of the brain and spinal cord may be affected, but the virus has a predilection for the grey matter at the base of the brain and in the brain-stem.

Microscopical appearances, according to Greenfield, in the acute stage are intense congestion of the capillaries and small veins with perivascular

infiltration, or cuffing of the latter by lymphocytes and plasma cells. There is a diffuse infiltration of the cerebral substance with small round cells, and degenerative changes of nerve cells. In the chronic stage, the inflammatory perivascular infiltration is either absent or patchy, and the characteristic lesion is a gradual degeneration and disappearance of nerve cells with or without neuronophagy. The clinical manifestations are related to the areas involved; mental disorders to lesions of the cortex and centrum ovale; the Parkinsonian syndrome to lesions of the substantia nigra; respiratory disorders to damage of centres in the brain-

FIG. 437.—BOY, AGED FIFTEEN YEARS: ACUTE ONSET EPIDEMIC ENCEPHALITIS WITH GRADUALLY INCREASING PARKINSONISM.
(From a photo supplied by Dr. M. Critchley.)

stem, and obesity, polyuria, somnolence and narcolepsy to the lesions of the hypothalamic area.

Symptomatology.—In the period of epidemic visitation, the disease was divisible into acute and chronic stages. The acute stage was sometimes abrupt but more often gradual. Symptoms of nasopharyngitis, pains in the spine and head, slight fever, drowsiness and a transient diplopia might suggest a diagnosis of "influenza," or more characteristic symptoms appeared, ocular paralyses, lethargy and disturbances of sleep rhythm. Ocular symptoms include blurred vision, diplopia, ptosis, nystagmus, inequality and irregularity of the pupils, and disturbances of conjugate movements and of accommodation and convergence. A common cranial nerve palsy was facial paralysis. Lethargy, sometimes amounting to a

deep somnolence, was more common in the acute stage than a state of irritability and hyperkinesis, combined with choreiform and myoclonic jactitations affecting one or several muscle groups of the trunk and limbs. Dysarthria, dysphagia, ataxy, frequent yawning and hiccoughs were common symptoms. The usual disturbance of the sleep rhythm was somnolence by day and restful wakefulness by night. Convulsions were uncommon except in young children. The acute stage lasted for a few days to several weeks, in which period the ocular pareses and myoclonic movements tended to disappear.

The chronic stage followed immediately upon the acute or made its appearance after a variable period, even of several years. Recently, symptoms of the acute stage have usually been so slight as to escape notice, and often the chronic stage alone is recognized. It is usually characterized by one or more of the following symptoms: a hypertonic state of general muscular rigidity, with a mask-like face and persistent salivation (Parkinsonism), a hemiplegia of slow onset, disturbance of sleep, involuntary movements, respiratory arrhythmias and tics, oculogyric crises or tonic fixation of the eyes in lateral or upward positions for seconds or minutes, obesity, polyuria, or narcolepsy. In children especially, mental deterioration either in conduct or intellect, or in both, a simple sluggishness or hebetude, is a frequent after-effect. The sequelæ of epidemic encephalitis form the most distressing feature of the disease.

The cerebro-spinal fluid is clear, colourless, not under pressure, and contains cells from 5 to 100 small lymphocytes per c.mm., and normal glucose and chloride percentages.

Prognosis.—Cases with severe general symptoms at the onset often prove rapidly fatal. In children, a higher mortality among females has occurred. In the chronic stage, paralysis of pyramidal type and Parkinsonism usually persist indefinitely. In the Annual Report of the London County Council of 1926, of the cases under sixteen years of age for the preceding seven years 111 were fatal, 119 recovered completely, twenty-three had slight and thirty-eight severe late effects, and seventy-five were wholly incapacitated.

Treatment.—There is no specific treatment. In the acute stage, phenobarbitone or chloral hydrate are useful. In the chronic stage, hyoscine by mouth, grain 1/200, of tincture stramonium, 5 minims, thrice daily, rising to limit of tolerance, or pills of dry extract of stramonium, 2 grains, twice daily, help to reduce Parkinsonian rigidity. Ephedrine, ½ grain, or amphetamine, 5 mgm. in conjunction with drugs of the belladonna group, gives relief to cases with oculo-gyric crises in about 50 per cent. of patients (Hoffman). In mental disorders in adults certification may be necessary, and in children institutional treatment.

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PINK DISEASE

(AN ENCEPHALO-MYELITIS)

SYNONYMS.—Trophodermatoneurose (Selter), Vegetative neuropathy (Feer), Acrodynia, Selter-Swift-Feer's disease.

Introduction.—A disease of infants and young children, characterized by symptoms of disturbance of the vegetative nervous system, and often complicated in chronic cases by signs of a spinal neuronitis. The condition presents so distinctive an appearance that its absence from the literature prior to 1903 leads to the view that it is a new disease. The earliest cases to be recorded were those of Selter in Germany (1903). Subsequently it has been described in Australia, North America and most European countries ; at first by Swift (1914) and Wood (1921) in Australia ; Bilderback (1919) in America ; Parkes Weber (1921) and Thursfield and Paterson (1922) in Great Britain : Comby (1922) and Haushalter (1925) in France ; and Feer (1923) in Berlin and later in Zürich.

Pathology.—In only a small number of fatal cases has the histopathology been thoroughly examined. In five fatal cases, Blackfan and McKhann stated nothing was found which could not be related to the effect of a terminal complicating infection. Greenfield and Paterson described a diffuse infiltration with small round cells of glial type, rather than lymphocytes, of the spinal cord, especially in the lumbo-sacral region, and degeneration of the myelin sheaths of the peripheral nerves, more marked in their distal than proximal parts. In a chronic case, spinal ventral horn cells showed a degenerative "axonal" reaction, particularly those supplying the distal portions of the limbs. This small-celled infiltration of the cord was found in all seven fatal cases examined by Wyllie and Stern and degeneration of peripheral nerves in four. In two cases they found, in addition, some cellular infiltration in the cerebral cortex, basal ganglia, brain-stem and medulla. Others have recorded lesions in the infundibular and hypothalamic areas, which could be taken to explain the predominant feature of disturbance of vegetative centres, but, as Cornelia de Lange has shown, the normal histology of this region in infants bears a close similarity to what some authors have claimed as abnormal. Evidence, however, of a frank encephalo-myelitis was present, of greatest intensity in the basal ganglia, on post-mortem examination in a case of Lapage, and clinically in two other cases described by Rocaz, and by Neale (reported before the British Pædiatric Assoc., 1943).

An important finding in a few cases dying suddenly with signs of heart failure has been degeneration of the vagus nerve. This has been proved histologically in two such cases examined at The Hospital for Sick Children, Great Ormond Street.

It is notable that the clinical symptoms in pink disease are much in excess of the apparent severity of the pathological lesions. Allocating the signs of vagal and sympathetic dysfunction to centres in the basal and subthalamic nuclei and substantia nigra, Kuiper and other authors consider the disease to be mainly encephalitic, or a vegetative syndrome of the di- and mes-encephalon.

Ætiology.– The disease most commonly occurs between the ages of four months and two years, but the onset has been as early as the third week and as late as the seventh or eighth year. The seasonal incidence in Europe is greatest between December and April. Both sexes are alike affected, in breast- as well as artificially-fed infants, either of urban or rural domicile. There is no evidence that diet or lack of vitamins plays any part in the causation of pink disease. Idiosyncrasy to mercury, usually in the form of calomel, had been put forward as a possible cause (Fanconi and Botsztejn, 1948; Warkany and Hubbard, 1948).

Many cases are sporadic, but a tendency is often noticeable to grouping by locality—foyers épidèmiques, inseln—although proof of contagion is lacking. A period of incubation is unsettled. In some cases an infective origin is suggested by a prodromal respiratory catarrh.

Consideration of the initial respiratory catarrh, the regional outcrop of cases, the presence of a moderate increase of cells in the cerebro-spinal fluid in the early stages of the disease in some cases, the character of the nervous lesions, discloses so much similarity to other forms of encephalomyelitis of virus origin that opinion in this country, America and France is in favour of an infective agent, probably a neurotropic virus.

Symptomatology.—The syndrome of pink disease wears so distinctive a stamp that the diagnosis is usually apparent at a glance. The conspicuous symptoms are *psychical*, insomnia, melancholy and agitation; *cutaneous*, "raw-beef" cold hands and feet, prurigo, a pink erythematous patch on nose and both cheeks, papulo-macular and sudaminal rashes and excessive sweating; and *nervous*, photophobia, muscular hypotonicity, and in chronic cases, loss of tendon reflexes and anæsthesia to pinprick, Besides the complete or neuro-cutaneous variety, Rocaz speaks of a nervous form in which the rashes and cutaneous cyanosis are almost lacking. Abortive cases are common, and relapses after a period of months have been noted. The disease runs a chronic course, often with periods of partial remission, and lasts commonly for several months to more than a year.

A history of a prodromal febrile illness with respiratory or intestinal catarrh is obtained in many cases. Next it is noted that the child's disposition alters; he becomes acutely miserable, irritable, whines continuously, loses all appetite and sleep is disturbed. He shuns the light with screwed up eyes and often takes up a knee-elbow position in bed, rubbing his face in the pillows, or gnawing at his fingers, or rubbing his legs together. The photophobia is usually unaccompanied by conjunctivitis. An excessive discharge of nasal mucus and of saliva is seen in many cases. The hands and feet become bluish-red, slightly swollen, glazed and cold, and desquamate in a patchy scarlatinal fashion. Bluish-red papules are often present on the distal parts of the extremities. Sweating is often a prominent symptom, and may lead to a diffuse miliary sudaminal rash. Meanwhile in an uncomplicated case, the temperature remains normal or slightly subnormal, the pulse rate is accelerated up to 140 to 180, and, as Feer showed, the blood pressure is raised, 110 to 120 mm. Hg. The blood-sugar may be raised (Blackfan and McKhann).

The muscles become markedly hypotonic and waste considerably.

The child may be unable to stand up. Trophic disturbance is noticeable in many ways; skin lesions show little sign of healing; the nailbeds may become unhealthy from sucking and biting; the eyelashes often become excessively long, shedding of the hair and of the nails has occurred; very rarely the teeth become loosened and even drop out; gangrene of the finger-tips has been recorded (Parkes Weber, Debré and Petot).

The symptoms of pink disease, as Feer first pointed out, can nearly all be related to disturbance of the vegetative nervous system, vagus and sympathetic. Secondary low-grade infections of the ear, lungs and renal pelvis with accompanying pyrexia are common and account for most of the mortality, which Muller placed at about 5 per cent. In rare instances sudden death has occurred from cardiac failure due to vagal degeneration. Cases with convulsions and other encephalitic signs have been described. The white cell count of the blood is usually normal in the absence of secondary infection. A mild pleocytosis, 15 to 50 small lymphocytes per c.mm., has been found in the cerebro-spinal fluid at the beginning of the disease.

The majority of cases recover after a period of several weeks or months and in the latter stages of the disease the cyanosis or capillary stasis of the hands and feet becomes phasic, coming and going intermittently.

Treatment.—As in other diseases of undetermined agency, many forms of treatment of short-lived currency have been employed. Good nursing is a first essential, as careful and frequent feeding, even by stomach tube, is needed to combat the anorexia. To prevent scratching, light cardboard splints are applied to the limbs, the skin surfaces are well covered with calamine lotion, and the child is clothed in cotton or silk. For the itching, small doses of phenobarbitone are useful, and for sleeplessness, chloral and bromide as required. Some writers have found ultra-violet rays useful in reducing the sweating and the severity of the itching. Feer recommends atropine by mouth, 5 to 15 drops of a 1 per cent. solution two to four times a day, but tolerance is best tested with smaller initial doses. A composite of atropine, ergotamine and phenobarbitone (bellergal) has also been used with success in symptomatic treatment in small graduated dosage.

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CONGENITAL CEREBRO-SPINAL SYPHILIS

Introduction.—The manifestations of congenital syphilis in the nervous system of infants and children are many and varied. It will give rise to a meningitis, hydrocephalus, amentia and diplegia in infants,

and to general paralysis, tabo-paresis and tabes dorsalis in older children. A luetic inheritance, however, may only be betrayed by an isolated disturbance of the central nervous system. Pupillary defects, the Argyll-Robertson pupil, or retino-choroiditis may be solitary signs. Ptosis and paralysis of the external ocular muscles are uncommon signs in children and inner ear deafness rarely occurs. Epilepsy, *petit* or *grand mal*, is sometimes of syphilitic origin. In all its forms, congenital syphilis is less often seen than formerly. Reasons for this are the earlier and more thorough treatment of syphilitic adults and especially the antenatal treatment of mothers, which is becoming fortunately more widespread in its application.

Other stigmata of congenital syphilis in childhood includes such signs

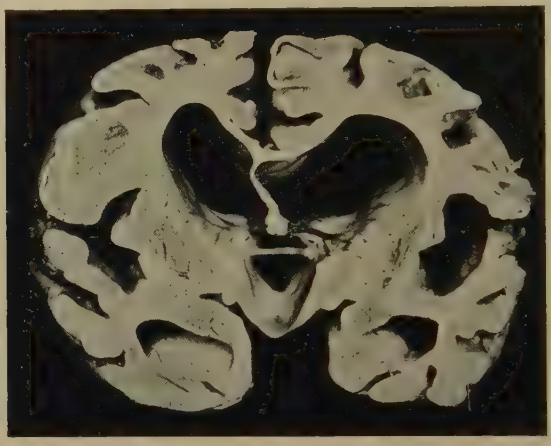

FIG. 438.—VERTICAL SECTION THROUGH THE BRAIN OF AN INFANT WITH SYPHILITIC MENINGITIS.

Note the wasted condition of the convolution, the dilatation of the ventricles, and the area of softening and cavity formation between the superficial and deeper layer of the cortex. This is well seen in the convolution to the right of the longitudinal fissure.

as stunted growth, interstitial keratitis, saddle-back nose, Hutchinsonian teeth in the second dentition. The manifestations of congenital neuro-syphilis are so protean that the nature of their causation is often unsuspected. Frequently it is some detail in the parental history which suggests the diagnosis; paralysis in one or other parent, or a maternal history of stillbirths and miscarriages.

The Wassermann reaction (see ch. XXXIV) is of the greatest assistance, as it is positive in nearly all cases of neuro-syphilis in the child. A positive reaction in the blood or cerebro-spinal fluid without any clinical evidence of syphilis is frequently found in the children of syphilitic parents. It is reasonable to give such cases the benefit of anti-syphilitic treatment, as otherwise they will be potential candidates at a later age for the development of paresis or tabes dorsalis.

(1) IN INFANCY.—Syphilitic meningitis or meningo-encephalitis is a

chronic disease. In nine out of fifteen cases recorded by Ranke the *Treponema pallidum* was found. In the first months the infant appears healthy, but at such a time as he should begin to hold up his head, it is noticed that he fails to do so. It is also observed that the infant takes no notice of his surroundings. The head appears larger than normal, but no great degree of hydrocephalus develops. The limbs tend to become rigid and there is comparatively little power of movement. Fits may occur from time to time. The Wassermann reaction is positive in both blood and cerebro-spinal fluid.

Pathologically, the pia-arachnoid over the vertex is thickened and opaque, often adhering to the cortex from which it is separated with difficulty. The convolutions are shrunken and the sulci widened. On section, the ventricles are dilated, and there is a separation of the cortex from the deeper layers by loose areolar tissue which contains a milky or clear fluid.

(2) After infancy, neurological manifestations of syphilis do not usually occur until about the eighth year, but, in the intervening period, optic atrophy and cerebral paralysis, such as hemiplegia, sometimes appear following one of the acute infectious fevers, which possibly acts as an agent stirring a latent syphilitic infection into activity.

(3) Juvenile general paralysis rarely begins before the eighth year. A child that has been normal in physical and mental development alters in disposition, deteriorates intellectually, becomes irritable and subject to outbursts of temper, and is careless of personal cleanliness. Speech becomes halting and slurred. A fit may now occur, leaving weakness on one side of the body, which may pass off in a few days. Other symptoms are tremor of the lips, shaking of the limbs and an unsteady or spastic gait. Pupillary changes are commonly present, and optic atrophy and signs of tabes develop in a few cases (tabo-paresis). The degree of physical and mental weakness rapidly increases after successive epileptic seizures. In cases observed by Mott, two lasted only three months, two eighteen months, one a year, and one seven years. The Wassermann reaction is positive in blood and cerebro-spinal fluid, and the Lange curve is usually of the paretic type.

(4) Juvenile tabes is a much less common manifestation than general paresis. The onset is usually about the twelfth year, but may be delayed until the twentieth, or even later. The disease tends to run a prolonged course. Unequal pupils, Argyll-Robertson pupil, absence of knee- and ankle-jerks, unsteadiness of gait and sphincter weakness are the usual symptoms. Optic atrophy may be present, and aching pains in the legs occur of less severity than the lightning pains of the adult tabetic. Some cases resemble Friedreich's disease (p. 1332).

The Wassermann reaction can be negative in juvenile tabes dorsalis, though it may be found positive in one or other parent.

Treatment.—The aim of treatment is a serological reversal from a positive to a negative Wassermann, attained by spaced courses of intramuscular injections of organic arsenic and bismuth. Penicillin is used in treating congenital neuro-syphilis. For details of dosage of arsenicals,

bismuth, and of penicillin, in neuro-syphilis, see ch. XXXIV. The results of the treatment in children of neuro-syphilis, except in the case of juvenile tabes, fall far short of those obtained with adults. The prognosis is especially poor in cases of syphilitic meningo-encephalitis.

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TETANUS

The tetanus bacillus, or *Clostridium tetani*, is an anærobic, motile, spore-forming organism, prevalent in cultivated, manured soil, which produces an exotoxin having a highly poisonous, strychnine-like action upon cells of the central nervous system. Infection commonly arises through the contamination of wounds with the spores, but it may occur through carious teeth, or umbilical sepsis at birth –tetanus neonatorum. Sepsis at the portal of entry, or the presence of a foreign body, facilitate the growth of the organism. The exotoxin is produced locally and either reaches anterior horn cells along neighbouring peripheral motor nerves, or passes by lymphatics into the general circulation, thence by diffusion

FIG. 439 and 440.—TRISMUS IN TWO CASES OF CEPHALIC TETANUS.

reaching motor neurons at any point. The incubation period is from one to twenty-one days or more, commonly seven to fourteen.

By a diffuse circulatory spread, the shorter neurons provide the earliest clinical manifestations—trismus, risus sardonicus, stiffness of the jaw, neck rigidity, and dysphagia. Spasm next extends to the abdominal and spinal muscles and to the limbs. At first and in mild cases the condition is one of tonic rigidity, but severe cases at a later stage are complicated by paroxysmal or clonic exacerbations, in which jaw-clenching, opisthotonos, severe muscular pains, fixation of the chest with respiratory arrest and cyanosis, and profuse sweating occur. Hyperpyrexia is an ominous sign. Passive movements and efforts to feed the patient often provoke the spasms.

In local or ascending tetanus the tonic rigidity first appears in muscles contiguous to the wound of entry, but may spread and become generalized. Cephalic tetanus is a local type, usually mild in children, arising from an infected tooth-socket, in which spasm and paralyses of muscles supplied by the cranial nerves predominate, third, fifth and seventh.

Treatment.—For purposes of *prophylaxis*, 1,500 international units of antitoxin is the usual dose. For *immediate* treatment, 50,000 to 100,000 units in a single dose intravenously is best (Cole). There is no evidence that the antitoxin by the intrathecal route reaches the nerve cells more rapidly than by venous injection. Exotoxin in contact with nerve cells is fixed and unaffected by tetanus antitoxin, which must be injected as early as symptoms commence in order to neutralize unfixed or circulating exotoxin. The cleansing of an infected wound should not be undertaken until after antitoxin has been injected, as the surgical measures employed may liberate a local accumulation of exotoxin.

The most skilful nursing is required in feeding and to avoid as far as possible external stimuli provocative of reflex spasms. The patient should be nursed on a water-bed in a darkened room. When trismus and stiffness of the jaw make feeding difficult, an intranasal catheter can be introduced into the stomach, and the quantity of nourishment must be liberal to counteract the excessive expenditure of energy due to muscular spasms.

For the control of paroxysmal contractions, bromethol is the most suitable sedative, given rectally in doses of 0·07 to 0·1 c.cm. per kgm. of body-weight freshly made up as a $2\frac{1}{2}$ per cent. solution in warm water (not above 40° C.) Relaxation can thus be obtained for from one to several hours, and the repetition of the dose once or twice in twenty-four hours is governed by the signs of recurring muscular irritability. Bromethol exercises a depressant effect upon the centres of respiration, making the breathing shallow and rapid with onset of cyanosis. To counteract these signs, atropine, $\frac{1}{200}$ to $\frac{1}{100}$ grain is given subcutaneously, and if necessary 5 per cent. CO_2 in oxygen inhalation. To control severe spasms good results have been obtained with an intra-muscular daily injection of 0·25 c.cm. of tubo-curarine in oil (30 mgm. per c.cm.) for a child of ten years of age. In less severe cases, paraldehyde, 60 to 180 minims, per rectum, may have sufficient sedative effect, or pentobarbitone, half a grain per stone bodyweight, by mouth.

In the **prognosis,** Cole refers to a relatively long incubation, over seven days, and "period of onset," between appearance of trismus and first clonic spasm, more than two days, together over nine days, as a favourable indication for recovery. With a period of onset of less than forty-eight hours, death usually occurs within six days, despite all forms of treatment. When the clonic spasms have ceased, the state of tonic rigidity may persist for several weeks. A useful sedative for the tonic state is phenobarbitone. On recovery from tetanus, the functions of the motor neurons become fully restored.

REFERENCE

Cole, L. (1942). *Brit. med. J.*, **2**, 550.

LEAD ENCEPHALOPATHY

The absorption of lead by children comes chiefly from the sucking of lead nipple shields (Gordon and Whitehead), and from nibbling lead-painted toys, furniture and woodwork. Nervous complications usually take the form of an acute intoxication—meningo-encephalopathy—rather than a chronic poisoning such as peripheral neuritis. Between the years 1924 to 1933 as many as eighty-nine cases of lead poisoning admitted to the Boston Children's Hospitals were reported by McKhann and Vogt, of which seventy-two were between one and three years of age and in forty-five the symptoms were cerebral. Blackman reports twenty-two cases of lead encephalopathy in children, mostly between thirteen months and three-and-a-half years of age. In only two cases were signs of peripheral neuritis present in addition. The mortality in lead encephalopathy is high and the survivors commonly present nervous sequelæ, paralyses, mental deterioration, blindness, and convulsions.

Clinically, the child is usually debilitated, irritable and anæmic, and may have headache, mild pyrexia, constipation, abdominal pains and vomiting. The commonest nervous symptoms are twitching and frequent generalized convulsions. Stiffness of the neck, head retraction, delirium, papillœdema and paralyses of the limbs and of the ocular muscles may occur. Later the child passes into a state of stupor, or of coma.

The cerebro-spinal fluid is under greatly increased pressure and presents a raised protein percentage, sometimes xanthochromia, and a cell count of twenty up to one or two hundred per c.mm., usually lymphocytes, sometimes mainly polymorphonuclears in children. The presence of lead can be demonstrated in the fluid, in the blood and in the urine.

Pathology.—The brain is swollen and the convolutions flattened due to an intense degree of œdema. The meninges are œdematous, exudate and capillary hæmorrhages are found along the vessels in the cerebral substance. Necrosis and endothelial swelling occur in the arterioles of the meninges and of the grey and white matter, followed by cerebral atrophy due to ischæmia in non-fatal cases. An important point in diagnosis is the demonstration by X-rays of a dense shadow along the diaphyseal lines of the growing bones, due to the deposition of lead—tertiary lead phosphate—with condensation of the bony trabeculæ. The anæmia is hæmolytic in type, with reticulocytosis, nucleated red cells, and punctate basophilia. A blue line along the gums due to deposits of lead sulphide is seldom seen in children.

Treatment is mainly symptomatic, to reduce intracranial pressure by lumbar puncture, or by the intravenous injection of 25 to 50 c.cm. of a 25 per cent. solution of dextrose. Efforts to retain the lead in the bones and prevent its liberation into the blood stream are made by administering calcium as contained in a liberal milk supply, or by injecting intramuscularly 5 to 10 c.cm. of a 10 per cent. solution of calcium gluconate. Vitamin D should also be given. A calcium deficiency, or a febrile condition tending to produce an acidosis, favour the conversion of the

insoluble lead phosphate in the bones into the more soluble di-lead salt, and aggravate the condition (Rodgers, Peck and Jupe).

Lead encephalopathy is liable to be mistaken for spontaneous encephalitis, or for cerebral tumour. The state of debility, abdominal pain, and the anæmia are distinguishing features.

REFERENCES

Blackman, S. S. (1937). *Bull. Johns Hopkins Hosp.*, **61**, 1.
Gordon, I., and Whitehead, T. P. (1949). *Lancet*, **2**, 647.
McKhann, C. F., and Vogt, E. C. (1933). *J. Amer. med. Ass.*, **101**, 131.
Rodgers, T. S., Peck, J. R. S., and Jupe, M. H. (1934). *Lancet*, **2**, 129.

DEGENERATIVE CONDITIONS OF THE NERVOUS SYSTEM DUE TO AN AVITAMINOSIS

There are only three conditions to mention, and they seldom occur in Great Britain and rarely in children.

Pellagra.—Maize plays no specific part in the causation of pellagra, but subsistence on a defective diet lacking an extrinsic factor, the *pellagra preventing* fraction of vitamin B_2, known as nicotinic acid, is capable of producing the disease provided an intrinsic factor is also absent, often in association with gastric achlorhydria. Under apparently similar conditions only one member of a family may be affected. The disease occurs in this country sporadically, or as a sequel of some chronic intestinal condition, or among elderly mental defectives in institutions.

Cutaneous, alimentary and nervous symptoms develop. The dermatitis begins usually in Spring in sunshine as a rash resembling exaggerated sunburn on the face, neck, arms and legs, especially on areas of friction and exposure. Alimentary symptoms are cheilosis, stomatitis, gastritis and diarrhœa. The nervous symptoms are mental dullness or dementia, weakness and disorders of sensation of the limbs, legs more than arms, spastic paralysis, tremors, and the tendon reflexes, at first exaggerated, may be abolished. Convulsions occur in some cases.

Simpson recorded a case in a schoolgirl of thirteen years with onset in May of typical skin rashes and pains and weakness of the legs. A convulsion and later status epilepticus supervened and the child died.

Pathology.—In the brain, basal ganglia, and spinal cord there is chromatolysis of ganglion cells, tract degeneration with demyelination in the cord especially of the dorsal columns, and there may also be degeneration of the myelin sheaths of the peripheral nerves (Greenfield and MacDonald Holmes).

Treatment.—Careful nursing and administration of nicotinic acid, 100 to 500 mgm., in small divided doses daily. It is advisable later to supply also other fractions of the B complex, riboflavin and aneurine.

REFERENCES

Greenfield, J. G., and Holmes, J. MacD. (1939). *Brit. med. J.*, **1**, 815.
Simpson, R. E. H. (1940). *Lancet*, **2**, 589.
Stannus, H. S. (1939). *Brit. med. J.*, **1**, 950.

Beriberi occurs as a result of the consumption of a diet wholly lacking the antineuritic vitamin, B_1. The description of infantile beriberi in a Pacific island by Bray showed that the breast-fed infants only suffered and the nursing mothers had latent beriberi from a diet devoid of vitamin B. This vitamin appears to be necessary for carbohydrate metabolism, which if incomplete allows a breakdown-product, pyruvic acid, to accumulate and act as a poison to nervous tissue. Stannus considers that modified cases possibly occur in this country. There are cardiac symptoms, tachycardia, dilatation, signs of failure and general anasarca, and nervous symptoms of paræsthesia, muscular tenderness, weakness and wasting, and loss of reflexes.

Pathology.—The evidence of peripheral neuritis consists of degeneration of the myelin sheaths and to a less extent of the axis cylinders.

Treatment consists in supplying aneurine, 15 to 25 mgm. intramuscularly, and giving yeast and when practicable a diet of vegetables, butter, liver, and other substances rich in vitamin B_1.

REFERENCES

Bray, G. (1928). *Trans. roy. Soc. trop. Med.*, **22**, 9.
Stannus, H. S. (1942). *Lancet*, **1**, 755.

Wernicke's encephalopathy.—Campbell and Russell considered that the acute superior hæmorrhagic polio-encephalitis of Wernicke (1881) may depend upon an insufficient supply of aneurin or B_1, and possibly of nicotinic acid. In their study of twenty-one cases, one being $3\frac{1}{2}$ years old, the condition usually occurred as a terminal complication of other diseases chiefly of a gastro-intestinal type, which is suggestive of a defective absorptive capacity. The symptoms are disturbance of higher cerebral functions and of consciousness, of respiration, inequality and irregularity of the pupils, paralysis of conjugate movements, and in some cases signs of polyneuritis. The cerebro-spinal fluid may show a slight increase of protein. The duration of nervous symptoms was roughly seventeen days.

Pathology.—These authors described foci of vascular engorgement and parenchymatous degeneration most marked in the corpora mamillaria and other parts of the hypothalamus, peri-aqueductal grey matter of the midbrain and floor of the fourth ventricle.

Treatment.—When symptoms of mental confusion and others of a neuritic type arise in the course of another disorder, the possibility of Wernicke's encephalopathy should be kept in mind, and the effect of giving aneurine and nicotinic acid observed.

REFERENCE

Campbell, A. C. P., and Russell, W. R. (1941). *Quart. J. Med.*, **10**, 41.

FORMS OF PROGRESSIVE CEREBRAL SCLEROSIS ASSOCIATED WITH DEMYELINATION

The pathology of certain forms of degeneration of the nervous system is characterized by a *demyelinating process* of nerve fibres similar to that

mentioned under disseminated encephalo-myelitis. In the brain this process is usually bilateral, occurring mainly in the white matter, whereby the condition may be termed progressive centrolobar sclerosis. A glial sclerosis is secondary. Several forms occur mainly in infants and children under ten years of age, and may have a familial or sporadic incidence. There is no proof of an infective element in the pathogenesis, which is obscure.

Although the common element of demyelination is used to group these conditions on a broad basis, yet they have anatomical differences whereby the histologist is able to distinguish them. The clinician, however, is often restricted to recognize a degenerative condition, usually progressive, often familial, subacute or insidious more often than acute in onset, and characterized by mental deterioration, visual failure, spastic paralysis and epilepsy.

(1) **Schilder's encephalitis periaxialis diffusa (1912).**—A rare condition, sometimes familial (Symonds, 1928), occurring usually in children from the age of three years onwards and less often in adults. The onset is subacute, and the salient features of a typical case are failing vision, deafness, mental deterioration, unsteadiness, spastic paralysis, and in some cases epileptic seizures. Fever is absent, and headache is an inconstant symptom. The nature of the disease is difficult to recognize during life except in a typical case presenting fairly rapid failure of vision and deafness unassociated with any visible fundal changes or local otitic infection. The blindness and deafness are then of cerebral origin, but optic atrophy, or a mild degree of papillœdema, have been observed in some cases. A fatal termination occurs in a few months, or not for several years. Occasionally, a partial remission of symptoms, or even an arrest of progress of the disease, has been recorded. Clinical signs may be chiefly unilateral, where the morbid process affects mainly the central white substance of one hemisphere. The cerebro-spinal fluid may show a slight lymphocytic increase of cells and the Lange curve is sometimes of the paretic type.

Pathology.—The pathology has been fully described by Collier and Greenfield (1924). On section, the white substance of the brain, especially in the occipital lobes, is of a greyish-white or yellow tint, diffusely or in patches. In cases of rapid progress, the discoloured white substance is unduly soft, whilst in chronic cases it is hard from neuroglial overgrowth. Other foci are found in the optic tracts, pons, cerebellum and spinal cord. The cortical grey matter and a thin subjacent area of white substance retain normal appearances.

Microscopically, the characteristic feature is a widespread demyelination of the axis cylinders (periaxialis) in the white substance, secondary to which the axons themselves may be destroyed. Globoid cells containing lipoid substance are found in areas of recent softening. Usually symmetrical, the changes may be unilateral. There is scant evidence of an inflammatory causation, and familial cases suggest the demyelination may be due to a congenital disturbance of lipoid metabolism.

Diagnosis.—Clinically, the disease in adults can be mistaken for

disseminated sclerosis, unless characteristic symptoms of cerebral blindness and deafness are present. Cerebral tumours may be simulated in cases with headache, vomiting and some papilloedema. The commonly bilateral character of the physical signs and radiographical absence of widening of the sutures should help in preventing the mistake in diagnosis being made.

REFERENCES

Collier, J., and Greenfield, J. G. (1924). *Brain*, **67**, 489.
Schilder, P. (1912). *Ztschr. f. d. ges. Neur. u. Psych.*, **10**, 1.
Symonds, C. P. (1928). *Brit. J. Child. Dis.*, **25**, 83.

(2) **Krabbe's familial infantile form of diffuse cerebral sclerosis.**—Krabbe described five cases, with a familial incidence, of a diffuse demyelination of the white substance of the hemispheres and to some extent of the cerebellum and spinal cord in infants of four to six months of age. Death occurred after a period of four to twelve months, during which the following symptoms were observed: fever, screaming, convulsions, neck rigidity, opisthotonos, spastic paralysis with the lower limbs adducted and extended. Hearing was apparently normal. Optic atrophy was present in three cases.

Besides the diffuse demyelination, axis cylinder degeneration was present and neuroglial overgrowth. The grey matter and a layer of white substance underlying the cortex were relatively intact.

Taking into account the familial incidence, the similarity of pathology of this condition to encephalitis periaxialis diffusa, it is possible that Krabbe's cases represent an infantile form of Schilder's disease.

REFERENCE

Krabbe, K. (1916). *Brain*, **39**, 74.

(3) **Aplasia axialis extracorticalis congenita** is a heredo-familial disease of a chronic nature beginning in the early months of infancy, presenting extensive demyelination in the central white substance of the brain, with axis cylinder degeneration and glial sclerosis (Merzbacher). Pelizaeus, in 1885, described the condition in a family which ultimately had fourteen members affected on four generations. Batten and Wilkinson described similar cases in another family.

Symptoms were tremor, ataxy, nystagmus, spastic paralysis, mental retardation, and later, slow speech. The onset was in the first three months of life with a rapid progression up to about the sixth year, after which the condition in some cases became arrested and the duration of life not curtailed.

REFERENCES

Batten, F. E., and Wilkinson, K. D. (1914). *Brain*, **36**, 341.
Merzbacher, L. (1910). *Ztschr. f. d. ges. Neur. u. Psych.*, **3**, 1.

(4) **Progressive cerebral sclerosis in infants with primary degeneration of the oligodendroglia** (Greenfield).—In the two cases

recorded, both dying at the age of three years, the symptoms at onset at about eighteen months were progressive weakness of the limbs, followed by impairment of speech and vision. Terminally, the limbs were rigidly extended, the head retracted, and dementia present. The optic fundi were normal.

Post mortem, the demyelination in the white matter of the hemispheres involved those tracts in which myelination normally is delayed until after birth. Masses of mucinoid material and abnormal lipoid granules, with an absence of oligodendrocytes, which are supposed to have a nutritional value in the formation of myelin, suggest that the pathogenesis of this condition and possibly of the other infantile forms just described is an abnormality of lipoid metabolism in the formation of myelin.

REFERENCE

GREENFIELD, J. G. (1932–33). *J. Neurol.*, **13**, 287.

(5) **Neuromyelitis optica.**—The characteristic lesion in this condition is a diffuse rather than patchy demyelination of the spinal cord, of the optic tracts, chiasma and optic nerves (Walshe). Unlike disseminated sclerosis, the degeneration may advance to necrosis, cavitation and destruction of axis cylinders.

The age incidence is from the fifth to the sixtieth year, and a familial instance in identical twins has been recorded (McAlpine). Prodromal symptoms of headache, pyrexia and sore throat have been noted. The nervous manifestations are ocular and myelitic, either simultaneous, or one preceding the other by a few days or several weeks. Impairment of vision, usually in one eye at first and later in both, varies from bilateral central scotoma to almost complete amaurosis. When the lesion spreads close to the head of the optic nerve a " choked disc " occurs. The spinal symptoms are those of a transverse myelitis with spastic paraplegia, sensory impairment, and sphincter disturbance. The mortality is about 50 per cent. In non-fatal cases the condition is self-limited, relapses have not occurred, and recovery is almost complete, though pallor of the discs may be permanent.

REFERENCES

MCALPINE, D. (1938). *Brain*, **61**, 430.
WALSHE, F. B. (1935). *Bull. Johns Hopkins Hosp.*, **56**, 183.

(6) **Disseminated sclerosis.**—It is seldom that this disease is seen below the age of puberty, and some cases so diagnosed may have been instances of acute disseminated encephalo-myelitis. Ford, however, mentions its occurrence in children between the ages of nine and fifteen years.

In the chronic stage, histology shows the familiar patches of *sclérose en plaques*, but in the acute stage, as described by Perdrau and others, there are focal or disseminated areas of demyelination accompanied by some perivascular cellular infiltration.

Clinically, the condition is marked by remissions and chronicity, and presents optic neuritis, temporal pallor of the discs, impaired vision, nystagmus, spinal signs of paraplegia, subjective more often than objective sensory changes, intention tremor, ataxy, and sphincter disturbance.

Two cases in children aged seven and seven-and-a-half years have been observed, with negative Wassermann reactions, in which a diagnosis of disseminated sclerosis was clinically acceptable. In the first, a girl, at seven years, sudden amblyopia and diplopia developed, accompanied by nystagmus, inequality of the pupils, and later by ataxy, intention tremor, paræsthesia and weakness of one leg with an extensor plantar response. There followed a remission for several years, with disappearance of all symptoms except slight impairment of vision of one eye. In this eye there was temporal pallor of the disc. Later, at the age of thirteen years, there was a recurrence of symptoms more aggravated and of greater extent. The other case, a boy of seven-and-a-half years, rather suddenly developed a staggering gait, holding his head to one side, had temporary difficulty with micturition, and had some headaches, vomited a few times and was somewhat lethargic. A month later he complained of intense stabbing pains with some flushing of the right half of the face, had some nausea and held his head over to the right side. A few days later he noticed the sight of the right eye was defective in that he "lost things." There was, in fact, a large scotoma in the right visual field, which cleared up in a period of three weeks. He also had some ataxia, left-sided more than right, and a tendency to a left extensor plantar response. Gradually all the symptoms disappeared and three years later he was normal, except for pallor of the right disc.

REFERENCES

Ford, F. R. (1937). *Diseases of the Nervous System*, London, 268.
Perdrau, J. R. (1928). *J. Path. Bact.*, **31**, 17.

CEREBRAL DEGENERATION OF EXTRAPYRAMIDAL TYPE

Interference with the functions of the corpus striatum gives rise to disturbances of tone, rigidity, tremor and choreo-athetosis. Symptoms of this nature have already been noted to be specially common in epidemic encephalitis, the virus of which disease has a predilection for the nuclei of the basal ganglia. Other conditions in children in which extrapyramidal signs predominate are the *état marbré* of the Vogts, Wilson's hepato-lenticular degeneration, torsion spasm, and kernicterus.

(1) The Vogts applied the term **status marmoratus** to a curious marbled or spotted appearance of the corpus striatus seen in certain cases following difficult birth. The supposition is that as a result of asphyxia neonatorum, vascular lesions are mainly confined to a disintegration of the nuclei, putamen and globus pallidus. In children surviving such injuries at birth, spasticity and choreo-athetosis may develop without signs of pyramidal lesion, paralysis, or extensor plantars. Paterson and Carmichael have described a form of familial cerebral degeneration chiefly affecting the lenticular nuclei.

REFERENCES

Paterson, D., and Carmichael, E. A. (1924). *Brain*, **47**, 207.
Vogt, C., and O. (1919–20). *J. Psych. u. Neurol.*, **25**, 631.

(2) Hepato-lenticular, or progressive lenticular degeneration.—This disease, first described by Gowers as "tetanoid-chorea," has been fully investigated by Kinnier Wilson (1912). A notable feature of the disease is the association of cirrhosis of the liver with progressive degeneration of the lenticular nuclei. Young people have chiefly been affected, between fifteen and twenty years of age, or as early as the eighth year, often in families, but evidence of a congenital or hereditary tendency is not forthcoming. It is essentially and chiefly a disease of the extrapyramidal motor system characterized by involuntary movements, usually of the nature of a generalized tremor, less often athetoid, dysarthria,

FIG. 441.—PROGRESSIVE LENTICULAR DEGENERATION: PHOTOGRAPH OF BOY AGED TEN SHOWING THE SPASTICITY, CONTRACTURES AND OPEN MOUTH—CHARACTERISTIC FEATURES OF THIS DISEASE.

(From a photograph supplied by Dr. Wilson.)

dysphagia, muscular weakness, rigidity and contractures, and progressive emaciation. Emotionalism is usually present, and symptoms of a mental nature. The disease is progressive, and after a longer or shorter period fatal.

ÆTIOLOGY.—Stanley Barnes and Weston Hurst consider that the cirrhosis is the result of repeated attacks of acute or subacute hepatitis. Symptoms of the hepatic disturbance may be entirely absent, but in some cases the onset of the nervous symptom has been preceded by attacks of biliousness, "migraine," or of vomiting, fever, diarrhœa, and even jaundice and ascites. The method of involvement of the nervous system is unknown, but it is possible that a poison is elaborated in the liver with a selective affinity for certain of the nuclei at the base of the brain.

PATHOLOGY.—The characteristic change is a bilateral shrinkage and

disintegration of the lenticular nuclei affecting the putamen more than the globus pallidus. The caudate nucleus and the frontal cortex are also involved.

Symptomatology.—A child that has had normal mental and physical health begins to have involuntary movements and tremor increased by excitement and voluntary effort. Besides the tremor, a progressively increasing rigidity of the limbs and trunk develops. This also affects the facial muscles which, with disturbance of emotional control, gives rise to a fixed and fatuous expression in which the mouth is usually

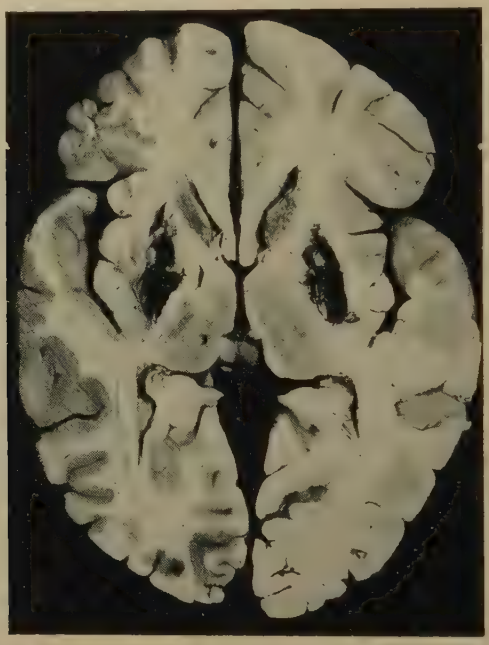

Fig. 442.—Progressive Lenticular Degeneration : Horizontal Section through Hemispheres, showing Bilateral and Symmetrical Cavitation of the Lenticular Nuclei.

(From a photograph by Dr. Wilson.)

open, and the child laughs or cries on little provocation. The acts of swallowing and articulation are interfered with.

The tremor and involuntary movements disappear during sleep. A gradually increasing rigidity of the muscles takes place, but the muscular power is often strikingly good in spite of the general state of emaciation. The tendon reflexes and the plantar responses are normal. The disease progresses slowly to a fatal termination in two to seven years, less often rapidly in a period of a few months.

REFERENCES

Barnes, S., and Hurst, E. W. (1925). *Brain*, **48**, 278.
Wilson, S. A. K. (1911–12). *Ibid.*, **34**, 295.

(3) **Dystonia musculorum deformans, or torsion spasm.**—This rare condition is characterized by spasms of increased muscular tone accompanied by involuntary movements of a twisting or writhing nature affecting the neck, trunk and proximal portions of the limbs. There is no evidence of pyramidal disease, the tendon reflexes are normal, or diminished, and sphincter and sensory disturbances absent. Intelligence and speech are unaffected, though the patient is rarely able to speak during the spasms. The involuntary movements at first appear on one side in the arm or leg before all four limbs and the trunk become

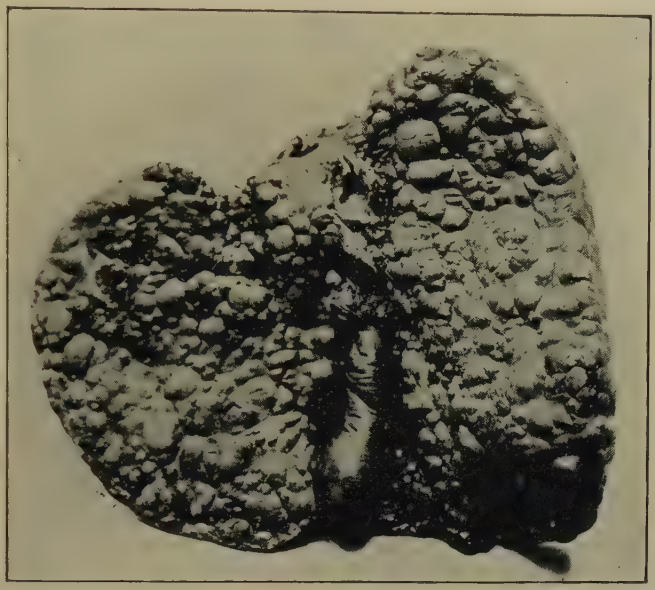

FIG. 443.—PROGRESSIVE LENTICULAR DEGENERATION: PHOTOGRAPH OF LIVER SHOWING THE IRREGULAR CHARACTER OF THE CIRRHOSIS, MAINLY OF MULTILOBULAR TYPE.

Cirrhosis of the liver is a constant feature in cases of this disease.

(From a photograph supplied by Dr. Wilson.)

affected. They are aggravated by excitement and disappear during sleep.

About forty cases have been recorded, of which only five have been of non-Jewish parentage. Males are more often affected than females and the condition is often familial.

ÆTIOLOGY.—This *dystonia lenticularis* is not always of the same causation. It can occur as a sequel of epidemic encephalitis, and the familial cases possibly have the same pathogenesis as hepato-lenticular degeneration.

PATHOLOGY.—Of the few cases of torsion spasm which have come to autopsy, those of Wimmer and Thomalla both had cirrhosis of the liver as well as degenerative changes of the lenticular nuclei.

REFERENCES

Garland, H. G. (1932). *J. Neurol. Psych.*, **12**, 193.
Thomalla, C. (1918). *Zeit. f. d. ges. Neurol. u. Psychiat.*, **41**, 311.
Wimmer, A. (1925). *Rev. Neurol.*, **2**, 281.

Fig. 444.

Fig. 445.

Torsion Spasm.
(By courtesy of *Journal of Neurology*.)

(4) **Kernicterus, or nuclear jaundice.**—Jaundice of the brain, or nuclear jaundice, was first described by Smorl in 1904. This is a common consequence of the blood disorder, icterus gravis neonatorum.

Most cases prove fatal within the neonatal period. Clinically, jaundice is apparent at birth or on the first or second day after birth, followed soon afterwards by onset of pyrexia, tonic and clonic movements going on to convulsions with screaming, hypertonicity, and even opisthotonos between attacks. Death usually occurs about the fifth day.

Roughly, only about eight cases have been reported in children dying some months or years after the neonatal period with cerebral lesions to confirm the existence of neurological sequelæ of kernicterus (Fitzgerald, Greenfield and Kounine).

In these children surviving the immediate illness of the neonatal period the following clinical signs were present, involuntary movements of a choreo-athetotic type, muscular hypertonicity, or extrapyramidal rigidity. There was also usually emotional instability, mental retardation and visual impairment. Post mortem, in such cases degenerative changes are mainly confined to the basal ganglia, subthalamic nuclei, the cornu ammonis, and the cerebellar dentate nuclei (Zimmerman and Yannet).

REFERENCES

Fitzgerald, G. M., Greenfield, J. G., and Kounine, B. (1939). *Brain*, **62**, 292.

Zimmerman, H., and Yannet, H. (1935). *Amer. J. Dis. Child.*, **49**, 418.

AMAUROTIC FAMILY IDIOCY, TAY-SACHS' DISEASE; CEREBRO-MACULAR DEGENERATION

The characteristic feature in the pathology of this form of progressive cerebral sclerosis is a lipoid degeneration of the ganglion cells most marked in the cerebral cortex, cerebellum and the retina. The clinical signs are progressive mental deterioration, paralysis, and blindness, with symmetrical changes at the maculæ. The disease manifests itself in three forms—the infantile, the late infantile, and the juvenile, or cerebro-macular degeneration.

Ætiology.—The disease is of endogenous origin with a primary degeneration of *neuro-ectodermal* cells of the cerebral cortex (Schaffer) whereby they become distended with lipoid products in the form of cerebrosides, but chiefly of phosphatides, a stage between the composition of myelin and neutral fat (Schlesinger, Greenfield and Stern). The infantile form is mainly confined to the Jewish race. Consanguinity of the parents has frequently been noted, especially in the juvenile cases of non-Jewish origin, and the condition is probably inherited as a Mendelian recessive. Nicolo and Mandel both record cases of the infantile type in which the parents were first cousins without any Jewish antecedents.

A relationship has been claimed with Niemann-Pick's disease, also chiefly confined to the Jewish race, inherited as a recessive, and occurring in infancy. The feature of this disease is a disordered metabolism of lipoids with great increase of phosphatides, chiefly lecithin, collected in the typical " foam cells " in the enlarged liver and spleen. The disease is primarily one of *mesodermal* tissues, but in some cases *ectodermal* cerebral lipoidosis has also been present. The association in the same case of the Tay-Sachs' and of the Niemann-Pick's types of lipoid disorder is in favour of their close relationship. From the records of forty-two cases of Niemann-Pick's disease, Atkinson in nine noted the presence of a cherry-red spot at the macula, but without optic atrophy. In another condition—gargoylism—which may prove to be due to a disorder of lipoid metabolism, the neuropathology is similar to that of the juvenile

form of amaurotic idiocy, or cerebro-macular degeneration. Ashby, Stewart and Watkin considered that the lipoid in the brain consisted chiefly of the cerebrosides, phrenosin and kerasin (see p. 367).

Pathology.—The nature of the morbid changes is essentially the same in the infantile, late infantile and juvenile forms of amaurotic idiocy. Such differences as exist are explained by the different stages of cerebral

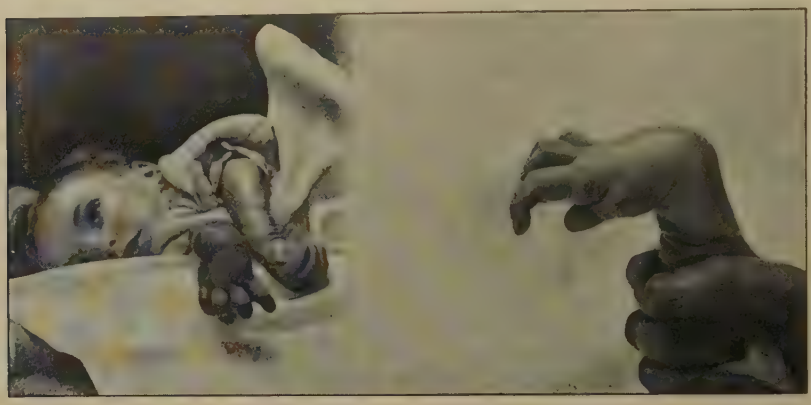

FIG. 446.—PHOTOGRAPH OF CHILD SUFFERING WITH AMAUROTIC IDIOCY, SHOWING THE POSITION OF HANDS.

FIG. 447.—PHOTOGRAPH OF A CHILD SUFFERING WITH AMAUROTIC IDIOCY.
Note the extended and pronated position of the arms and the retracted position of the head.

(With Dr. Carlill's and Dr. Mott's kind permission.)

development at which the degenerative changes begin. The ganglion cells present a ballooned appearance, being swollen with lipoids. The brain is of normal size, or slightly reduced, is harder than normal and shows some widening of the sulci. Relatively to the cerebrum, the cerebellum, especially in the juvenile type, often appears to be much reduced in size. The ganglion cells of the retina and their processes are also extensively degenerated.

Symptomatology. INFANTILE TYPE (Waren-Tay-Sachs').—The infant

at birth appears to be normal. Between the third and sixth months it becomes apathetic, less active, loses the power to hold up the head, or to sit, and ceases to take notice. Gradually the impairment of vision becomes more obvious and the eyes wander aimlessly about, the child taking no notice of its surroundings, but being susceptible to sounds. At this period the characteristic cherry-red spot is present at the macula, surrounded by a lighter halo, and the optic disc is white. At first the limbs tend to be flaccid, but later become rigid, adducted and extended with exaggerated tendon jerks and extensor plantar responses. The cerebro-spinal fluid is usually normal, or contains a few lymphocytes. The infant emaciates, convulsions occur, sucking and swallowing becomes more feeble, and death occurs after an illness of several months.

Late infantile type.—The onset of the disease is between the

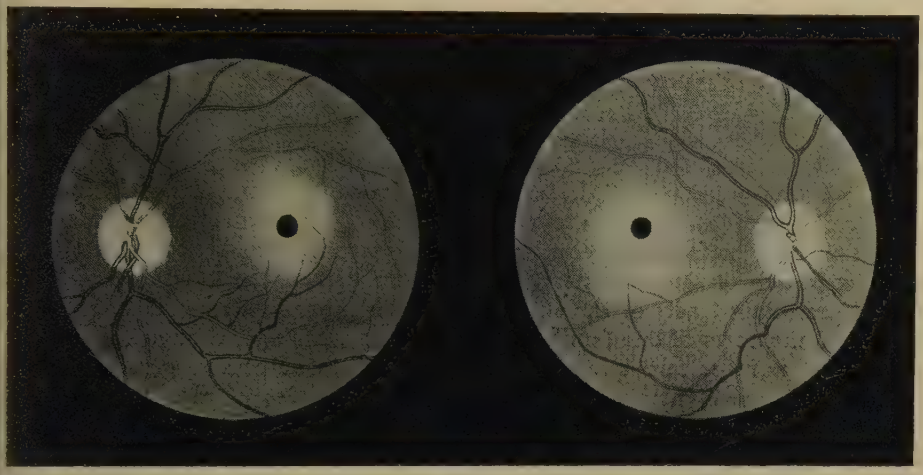

Fig. 448.—Appearance of the Region of the Yellow Spot in a Case of Family Amaurotic Idiocy.
(From Waren-Tay's original case.)

second and fifth years. The symptoms are similar to those of the infantile type, but at the macula a fine pigmentation is usually seen in place of the cherry-red spot. Only a few cases have been recorded by Torrance and others.

Juvenile type. (Cerebro-macular degeneration, Batten).—The time of onset is the sixth, seventh or eighth year, but may be as late as the fourteenth. In a family, the year of life at which symptoms commence is usually the same for each child affected.

Early symptoms are mental dullness and a falling off in school work. In looking at objects the head is turned sideways, so that the image may fall upon the periphery of the fundus. The child becomes irritable, dirty in its habits and inarticulate, but does not in the early stages manifest any weakness of the limbs. Gradually muscular weakness supervenes ending in rigid paralysis, the patient becoming bedridden and incontinent.

Convulsions occur once the disease is well established. The ocular fundi show atrophy of the discs and retinal degeneration, which commonly appears as a peppery stippling at the macula. The symmetrical changes, however, at the maculæ are not a constant feature, and the retinal pigmentation may be at the periphery. The duration of the disease is commonly five to eight years.

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FAMILIAL AND HEREDITARY ATAXIA

(Cerebral and spinal abiotrophies)

This interrelated group of heredo-familial ataxias is subdivided to suit the description of differences in its clinical presentation. Common features in most types are inco-ordination of voluntary movement, difficulty in maintaining equilibrium, and visual disturbance, based on degeneration of the optic nerves, cerebellum, olives, the long descending and ascending tracts of the spinal cord. The abiotrophy tends to affect several members of one family, usually at the same age, though the time of onset may be anticipated by several years in successive generations, or in successive members of one family. Examples of more than one type have occurred in one family. Males and females are alike affected, and transmission occurs more often through the normal than the affected members.

A classification modified from that suggested by Gordon Holmes is as follows :—

(1) Friedreich's ataxy—a combined system degeneration of the spinal cord.

(2) Spino-cerebellar ataxy, dependent on a primary degeneration of the spino-cerebellar tracts.

(3) Cerebellar ataxy, in which the morbid change is limited to the cerebellum and its immediate connections.

(4) Hereditary spastic paraplegia, in which the degeneration predominates in the pyramidal tracts.

The development of the familial diseases is governed by the laws of inheritance. Friedreich's ataxy is seen from the pedigrees gathered by Dresel and Hanhart to have the characters of a Mendelian recessive, about one affected to three sound members in a family. Consanguinity of two healthy parents, each holding the recessive element, favours the appearance of the disease in their offspring.

(1) **Friedreich's disease.**—Symptoms usually appear during the first

decade, but the child may have been backward in learning to walk, or may never have walked properly. Walking becomes worse gradually, the child staggers along, and seems in danger of falling, although it seldom does so. On attempting to grasp an object, the ataxia of the hand at once becomes obvious. The head and trunk are in almost constant movement, and while the child is standing it can be observed that the degree of contraction of the muscles is always varying. Speech is jerky and articulation often defective. The eyes often show a spontaneous nystagmus, or oscillations are only observed on bringing the eyes into a position of lateral deviation. The pupils commonly react to light. Ocular paralysis may be present and rarely optic atrophy with complete blindness. Mental defect can occur, but the manner in which the child talks and the slowness with which it does so, gives an appearance of mental defect which is more apparent than real.

Additional features are a lateral curvature of the spine, pes cavus and sometimes equinus, absent knee- and ankle-jerks and extensor plantar responses. The sphincters are rarely affected. A slight sensory impairment may be elicited over the periphery of the limbs. The disease is slowly progressive and may take several years to become fully developed. In the later stages wasting of muscles occurs and the deformity of the spine and feet becomes very obvious.

In some cases of Friedreich's ataxy, signs of pyramidal involvement outweigh those of degeneration of the spino-cerebellar tracts. In them, besides pes cavus and extensor plantar responses, the knee- and ankle-jerks are present and exaggerated and ataxy is either minimal or absent. Lightning pains have been described and when present should always suggest the desirability of testing the Wassermann reaction, as in some cases of congenital neuro-syphilis of the spinal cord, symptoms arise closely resembling those of Friedreich's ataxy.

Pathology.—The spinal cord often appears small, and degenerative changes are found in the posterior columns, the dorsal spino-cerebellar tracts and cells of Clarke's column, and in the pyramidal tracts.

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(2) **Spino-cerebellar ataxy** (Sanger-Brown).—The onset in the family reported by Sanger-Brown was between the ages of sixteen and thirty-five, but in the fifth generation the symptoms appeared in one child at the eleventh year. The type is characterized by progressive ataxy of the limbs, static ataxy, dysarthria, optic atrophy, with brisk knee- and ankle-jerks.

Pathology.—There is a primary degeneration of the spino-cerebellar tracts, slight changes in the dorsal columns, and the pyramidal tracts are usually unaffected.

REFERENCE

Brown, Sanger (1892). *Brain*, **15**, 251.

(3) **Progressive cerebellar ataxy.**—A slowly increasing ataxy, due to a primary degeneration of the cerebellum, can occur as a familial disease, beginning more often in adult life than in childhood.

A child who has made normal progress gradually loses the power of writing, begins to walk unsteadily and eventually becomes so ataxic as to be unable to walk. Speech alters, becoming slow and jerky. The general intelligence remains good. The disease runs a slowly progressive course.

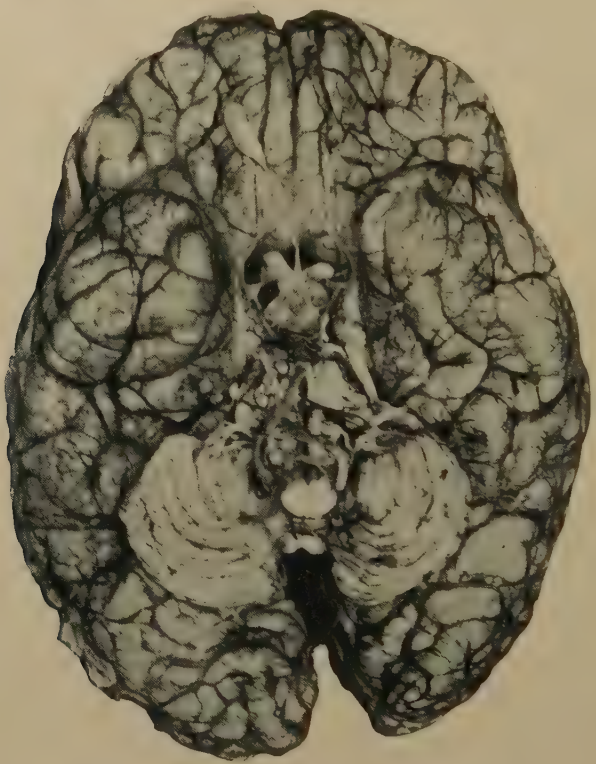

FIG. 449.—CEREBELLAR ATROPHY: PHOTOGRAPH OF BRAIN OF CHILD TEN MONTHS OLD, SHOWING CONGENITAL ATROPHY OF THE CEREBELLUM—A CONDITION FOUND IN MANY CASES OF CONGENITAL AND PROGRESSIVE ATAXIA, WHETHER OCCURRING IN FAMILIES OR SPORADICALLY.

PATHOLOGY.—The cerebellum is considerably reduced in size. There is degeneration of the cerebellar cortex and of the fibres connecting this with the central nuclei. The apparent cerebellar tracts are intact and there is no change in the spinal cord. The smallness of the cerebellum, Holmes states, must not be confused with agenesis of the cerebellum, with which there may be either no symptoms, or ataxia from the time of birth.

REFERENCE

HOLMES, G. (1907). *Brain*, **30**, 466.

(4) **Familial and hereditary spastic paralysis** is characterized by a slowly progressive spastic weakness starting in the legs and spreading to involve the trunk and arms. The tendon reflexes are exaggerated, pes cavus, ankle clonus, and extensor plantar responses, present without any affection of sensation, sphincter disturbance, or muscular wasting. The disease begins at any age, and may affect several children in a family. It is probable that the law of anticipation holds good, in that the children of an affected parent show signs of the disease at an earlier age than the parent.

Tremors of the trunk and arms, nystagmus, or optic atrophy, have been described, which makes a distinction difficult from one of the other forms of heredo-familial ataxia. Even starting in early childhood, the disease may not give rise to complete incapacity for ten or twenty years.

Pathology.—There is a degeneration of the pyramidal tracts in the spinal cord, not apparent above the medulla, and in some cases degeneration of the posterior columns, especially of Goll's column.

REFERENCE

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Family spastic paralysis, associated with amyotrophy, is an unusual form of progressive muscular atrophy affecting several members of a family. The clinical features are spasticity of the lower limbs and atrophy of the small muscles of the hands, which assume the claw shape. Pes cavus and equinus are present with exaggerated knee- and ankle-jerks and extensor plantar responses. Nystagmus may be present. Males and females are affected alike, and the disease transmitted from parent to child. Starting early in life, its progression is leisurely, so that many years elapse before incapacity is complete.

Pathology.—The chief changes are a degeneration of the pyramidal tracts and of the anterior cells of the spinal cord. In a case reported by Mass, the small size of the cerebellum was a striking feature.

REFERENCE

Holmes, G. (1905). *Rev. Neurol. Psychiat.*, **3**, 256.

MYELITIS

With the exception of poliomyelitis, nervous symptoms of an acute or subacute nature due to lesions limited in distribution to the spinal cord are rare in childhood. Acute myelitis alone, more often as an encephalo-myelitis, can occur as a complication of one of the infectious fevers, or spontaneously in acute disseminated encephalo-myelitis. In "influenza" epidemics an ascending myelitis is a rare complication, more often seen in adults than in children. Compression myelitis is usually caused by spinal caries, less often by spinal tumour. Cases of

myelitis, however, may arise for which no cause is found, though usually with a febrile onset and probably of an infective origin.

Hæmatomyelia.—Hæmorrhage into the substance of the cord is a condition which has been shown by Spencer to be not infrequently present in association with hæmorrhages in new-born infants. There is little doubt that the obstetrical procedure of traction in the infant during delivery is the essential cause of this form of hæmorrhage. The lesion of the cord is diffuse rather than localized and involves several spinal segments. Any portion of the cord may be affected, but the lower cervical and upper dorsal regions suffer most frequently. The same causes which give rise to hæmatomyelia may produce laceration of the spinal meninges and the latter may be torn without the cord showing signs of injury. In an analysis of cases observed in a period of six years which showed signs of cerebral or spinal paralysis attributed to birth injury, Crothers and Putnam found twenty-six cases of spinal as against 260 cases of cerebral palsies.

Symptomatology.—A high cervical hæmorrhage, interfering with the phrenics, proves fatal, but at lower levels, if the infant survives, the spinal lesion may express itself in various ways depending on the situation and severity of the hæmorrhage. Paralysis of the lower limbs may be spastic or flaccid with exaggeration or loss of the knee- or ankle-jerks. Some degree of anæsthesia below the level of the lesion is always present, and the loss of sphincter control is either complete, or there may be a reflex incontinence of urine. When the lesion affects the cervical enlargement, one or both arms is affected. A lesion in the lower part of the cervical cord gives rise to a flaccid paralysis of the arm, and a lesion higher up can produce both spastic and flaccid paralysis of different muscle groups in the same limb. The paralysis of the arm, however, may be due to an injury of the roots of the brachial plexus, either alone or in association with an injury to the spinal cord.

In addition to the brachial paralysis, another feature likely to be present when the hæmorrhage is in the lower cervical and upper dorsal region is paralysis of the cervico-sympathetic with narrowing of the palpebral fissure and a small pupil on the side of the lesion.

Apart from the cases due to injury to the cord at birth, hæmatomyelia rarely occurs. The condition, however, has been met in children and young adults. The only cause in these cases to which the hæmorrhage can be attributed may have been a fit of coughing, a sudden straining, or a great emotional excitement. Allbutt recorded a hæmorrhage into the cervical cord of an infant six months old. The only cause to which the hæmorrhage could be assigned was that the infant had been lifted suddenly so that the head fell sharply forwards. The signs of spinal hæmorrhage in such cases are of rapid onset.

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Ford, F. R., Crothers, B., and Putnam, M. C. (1927). *Birth Injuries of the Central Nervous System*, Baltimore.

Syringomyelia.—This disease is seldom seen in the pre-adolescent period, but cases have been described in children of less that ten years of age. The condition is usually sporadic, but may be heredo-familial, and is characterized pathologically by a gliosis and the formation of cavities in the region of the central canal. The morbid process may develop in any part of the cord or medulla (syringobulbia), but the situation most commonly affected is the lower part of the cervical enlargement. At this level it gives rise to wasting of the muscles of the hand, producing a *main-en-griffe*, and to spastic paralysis of the lower limbs, with dissociated anæsthesia –pain and thermal insensibility —of the arms and upper part of the chest, and cervico-sympathetic paralysis. A lateral lesion in the brain-stem above the decussation of the pyramids and of the fillet may produce a contralateral hemiplegia with dissociated anæsthesia of the paralysed side of the body.

Pathology.—Local neuroglial overgrowth precedes the formation of cavities, which are secondary to degenerative changes in the neuroglial tissue. An actual gliomatosis, or tumour growth, may occur within the cord and undergo cystic degeneration. The clinical features of such a case are indistinguishable from those of syringomyelia.

Treatment.—The application of X-rays to the affected level of the spine is the only therapeutic measure for which any success can be claimed.

SPINA BIFIDA

Spina bifida is the result of a congenital developmental defect of the neural canal, with want of union of one or more laminal arches commonly in the lumbo-sacral region, and sometimes associated with abnormalities of the overlying integument and of the underlying meninges and spinal cord. The defect can also occur in the thoracic and cervical regions. More often the condition is limited to a single member in a family, but may be hereditary. From a personal observation, spina bifida was found to occur in three successive infants in one family.

Five types of spina bifida are recognized : (1) a *meningocele*, a saccular meningeal protrusion containing only cerebro-spinal fluid ; (2) a *meningo-myelocele*, in which a part of the cord bulges into the sac and nerve roots are attached to the sac walls ; (3) a *syringo-myelocele*, when the central canal of the cord is ballooned out and the posterior surface of the cord lies just beneath the skin ; (4) a *myelocele*, when the medullary groove has failed to close and the central canal is in direct communication with the surface of the body ; (5) *spina bifida occulta*, which may cause no symptoms, or those produced by interference with the nerve roots of the cauda equina.

Except in the types meningocele and spina bifida occulta, paralysis of the sphincters and of the lower limbs is invariably present. The severer defects are incompatible with life, most cases dying in early infancy. The signs are flaccid paralysis of the legs, or flaccid below the knee and spastic above, absent tendon jerks, talipes varus and equinus,

sensory impairment and trophic disturbance of the skin, rectal and vesical incontinence, according to the extent of involvement of the spinal cord and its nerve roots.

In **spina bifida occulta** one or more arches have failed to close, usually in the lumbo-sacral region, which often happens without any signs of want of normal function of the spinal cord. The skin overlying the bony defect may be normal or marked by a lipoma, a dimple, pigmentation, or a patch of hypertrichosis. In a few cases a fibrous band may attach the dura through the vertebral defect to the overlying skin and adhesions to nervous structures may be present giving rise to paralysis. The nervous signs are either obvious soon after birth, or present to a minor degree, but later becoming accentuated from a traction upon the cauda equina and its roots owing to disparity in elongation of the spinal column and the cord. The signs are weakness of the legs, muscular wasting, sensory and trophic disturbances, often asymmetrical upon the two sides, and sphincter weakness, urinary more often that fæcal. The urinary incontinence occurs by day as well as at night.

Treatment.—In spina bifida occulta associated with paralysis the surgical liberation from tension of the cord, or spinal roots by reducing adhesions, offers good results. Surgical obliteration of the simple meningocele is not a difficult problem, but hydrocephalus sometimes develops following it. Spontaneous hydrocephalus is more often associated with meningo-myelocele, less often with meningocele. The explanation is the presence of an Arnold-Chiari malformation of the brain-stem, which is a protrusion down through the foramen magnum of a tongue-like process composed of cerebellar tissue and elongated medulla oblongata. The cavity of the fourth ventricle extends below the foramen magnum into the protrusion, and the foramina of exit for the cerebro-spinal fluid between ventricle and subarachnoid space are within the spinal canal. Owing to compression by this bulging in the upper cervical thecal space, the spinal and ventricular fluid is under tension in the form of a communicating hydrocephalus, but the fluid is hindered from reaching the subarachnoid spaces over the hemispheres. The soft tissues of the *meningocele* are capable of absorbing some of the cerebro-spinal fluid, so with their removal Russell and Donald suggest that intrathecal pressure rises in the presence of an associated Arnold-Chiari deformity and hydrocephalus is liable to develop.

REFERENCE

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SPINAL TUMOUR

The figures for the relative incidence of spinal growths in childhood vary greatly according to their source, whether general, or children's hospital, or neuro-surgical clinic. Horsley and Gowers from post-mortem records found it to be 10 per cent. in childhood out of fifty-eight cases

at all ages. Elsberg in a hundred cases states eleven were in the second decade and only one under ten years of age.

Tumours of the vertebræ in children are uncommon. Teratomata of the sacro-coccygeal area, also rare growths, are commonly present at birth and form a prominent external swelling. Spinal tumours may be extradural or intradural, extra- or intramedullary. In a review of ninety-nine proved cases of tumour within the spinal canal in children up to fifteen years of age, Hamby found intramedullary glioma, 23 per cent.; sarcoma, mostly extradural, 18 per cent.; neurofibromata, 7 per cent.; pial and subdural lipomas, 7 per cent.; subdural meningioma, 5 per cent.; sympathetic nerve tumour or ganglioneuroma, 4 per cent., and a few fibromas, cysts, hæmangiomas and unclassified growths. Chloromas, associated with the leukæmias, were present in 8 per cent. Cholesteatoma and the solitary tuberculoma are other rare spinal tumours (Craig and Mitchell). Ganglioneuromas, arising from the paravertebral sympathetic ganglia in the posterior mediastinum, or in the retro-peritoneal space, often have extensions into the spinal canal through the intervertebral foramen, the tumours having a dumb-bell or hour-glass formation.

The intramedullary astrocytoma, ependymoma, or other forms of glioma is the commonest type in childhood. Of two cases at Great Ormond Street, the ages were one year and five months, and two years and two months, and in both the neoplasm was situated in the upper cervical portion of the cord. When of cervical situation the arms are affected before the legs, the paralysis being of a mixed spastic-flaccid type in one or both upper limbs with muscle wasting and fibrillation. The *main-en-griffe* may be observed. A spastic paralysis gradually develops in the legs. Sensory loss begins just below the level of the lesion and is often dissociated. There may be a Brown-Séquard syndrome —loss of power on one side, loss of sensation especially to heat, cold, and pain on the opposite side. Sphincter control also becomes impaired. Root pains and spinal tenderness are usually absent and X-rays reveal no abnormality of the vertebræ. Extramedullary and extradural tumours give rise early to progressive pyramidal symptoms, root pains, and loss of sensation often dissociated to start with, as in the Brown-Séquard syndrome from lateral pressure, and later bilateral and to all forms of sensation as the compression increases.

The cerebro-spinal fluid may supply evidence of a block. Froin's syndrome of xanthochromia and a high protein content below the level of compression may be present. Sicard's method of localization by injecting lipiodol intracisternally and observing by radiography at what level in the spinal canal the opaque oil is held up may be employed.

Diagnosis.—Extradural tuberculoma tissue may compress the cord, but usually vertebral caries will be revealed by X-rays, even when spinal deformity is absent. For the symptoms of spinal arachnoiditis or meningitis circumscripta spinalis see page 1226.

Treatment.—The right line of treatment for spinal tumour is to attempt its removal. The intramedullary tumour can seldom be removed,

but a remarkable diminution of the paralytic symptoms often follows laminectomy, and at a second operation it may be found that the growth, if of a circumscribed type, has tended to deliver itself through the original posterior raphe incision in the cord.

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NERVOUS MANIFESTATIONS DUE TO SPINAL CARIES

Tuberculous caries of the spine is a common disease in children, and has its greatest incidence before the tenth year. The dorsal vertebræ are more often affected than the lumbar or the cervical. Injury to the cord is produced by the pressure of abscess or tuberculous tissue outside the dura, and by interference with its blood supply. Less often, the dislocation of a vertebral body is a cause of compression. In rare instances a tuberculous myelitis occurs as a result of the infection invading the cord itself.

Symptomatology.—Early symptoms are pains in the back, a disinclination to walk, and an attitude of slight flexion of the legs. A diagnosis of pseudo-hypertrophic paralysis may be suggested by the difficulty the child exhibits in rising from the ground into an erect position.

Signs of spinal compression are of gradual onset, predominantly motor, and manifested by weakness of the lower limbs, spastic gait, increased knee-jerks, ankle clonus and extensor plantar responses. The longest fibres in the cord are first affected, so that with a site of compression even as high as the cervical region a paraplegia precedes the onset of weakness of the arms usually by some months. As the pressure becomes more severe, there is a loss of sensation corresponding to the level of the lesion, and incontinence of urine and fæces. A third stage is sometimes reached in which the spastic condition of the legs is replaced by a flaccid paralysis, abolition of the knee- and ankle-jerks, and complete loss of all forms of sensation below the level of the lesion.

When caries is situated in the lower dorsal or lumbar region, the pressure comes directly on the lumbo-sacral enlargement and produces wasting of the muscles of the legs, loss of knee-jerks and an area of anæsthesia of the skin of a segmental or root distribution.

Caries at the level of the lower cervical and upper dorsal region may give rise to wasting of the muscles of the hands. The hand assumes the claw position, owing to weakness of the interossei. Cervico-sympathetic paralysis may also be produced by caries at this level.

The most careful examination of the back must be made in all cases of suspected spinal caries. Local tenderness and muscular rigidity on movement, and spinal deformity, are present in many cases, but in some paraplegia may be well marked without there being any deformity of the spine. In upper cervical caries there may be little or no local

tenderness, and the presence of muscular rigidity may be difficult to elicit. In an X-ray examination it is essential to include the whole vertebral column, otherwise a high cervical lesion in a case of paraplegia may be missed. The X-rays may fail to locate a bone lesion at the earliest stage of the disease, but in a suspected case it is advisable to keep the child at rest on a spinal board.

Treatment.—Rest in bed, fresh air, and a suitable form of extension to prevent deformity are indicated. Operation is sometimes necessary when the signs of compression increase in spite of treatment by rest and extension.

INFANTILE MUSCULAR ATROPHY OF SPINAL ORIGIN

WERDNIG-HOFFMANN'S DISEASE (PROGRESSIVE SPINAL MUSCULAR ATROPHY OF CHILDREN) AND OPPENHEIM'S DISEASE (AMYOTONIA CONGENITA)

Introduction.—Under the heading of infantile muscular atrophy, it is intended to include both Werdnig-Hoffmann's disease—progressive spinal muscular atrophy of children, and Oppenheim's disease—amyotonia congenita.

The close resemblance of the morbid changes in the nervous and muscular systems in the two conditions has frequently been commented upon. Greenfield and Stern, in order to emphasize the similarity in the histology of the two conditions, speak of their "anatomical identity." The anatomical pathology will be described later. Here, it will suffice to mention that the type of atrophy of the lower motor neurons and muscles seen in the two conditions is histologically indistinguishable. Their ætiological and clinical aspects, however, have been considered sufficiently divergent to make their recognition a matter of little difficulty. These will be described separately and afterwards critically compared.

FIG. 450.—CASE OF WERDNIG-HOFFMANN'S DISEASE.

Werdnig-Hoffmann's disease.—In its most characteristic form this disease is manifested by a progressive weakness and atrophy of muscles, affecting the proximal muscles in advance of the peripheral, the paralysis appearing at any time during the first year of life, but most often a few weeks after birth.

There is a steady progression of the paralysis to include all the muscles of the trunk and limbs and finally bulbar muscles become affected. Death commonly occurs in a matter of a few weeks to a few months.

The two sexes are equally affected. The condition tends to be familial. Werdnig gives an instance in which two brothers in a family of six were affected; Hoffmann, three families, in the first of which six out of fifteen were affected—four boys and two girls; a second family in which three were affected—two boys and one girl; and a third family of twelve in which eight were affected, and an unaffected female of this family had six children, three of whom were affected. Beevor describes a family of eight, in which four were affected.

The clinical features are more fully outlined in the following description: An apparently healthy and intelligent child who has made normal progress during the first few weeks or months of life begins, without any sudden onset, manifestation of acute disease, or any known cause, to lose power. If the child has already stood, it loses that power; it then loses the power of sitting up, and, finally, even the power of sitting up when placed in that position. The loss of power is first noticed in the muscles of the hip and then in those of the back, the shoulders, thighs, upper arm, forearm and leg muscles being successively affected in the order of parts as above mentioned. The paralysis of the proximal, as compared to the distal muscles, is a striking feature of the disease, for the child will move the fingers and toes while the arms and legs are completely paralysed.

The intercostal and abdominal muscles become affected with the other trunk muscles, whereas the power of the diaphragm always remains intact. The neck muscles become weak and the child is unable to hold up the head. Bulbar symptoms supervene, manifested by weakness of the muscles of the face and tongue. The ocular muscles are unaffected. Contraction of the limbs is rarely observed. Fibrillary twitching of the muscles may be present in some cases; but the amount of subcutaneous fat often covers up any wasting of the muscles and makes it difficult to observe such fibrillary twitching. All the deep reflexes are abolished and generally the superficial reflexes are also absent. There is, as a rule, no pain or tenderness. There is no alteration of sensation and the child usually responds to all cutaneous stimuli. The mental condition of the child continues unimpaired throughout the whole course of the disease, and the child takes notice, talks, laughs and swallows its food in a perfectly normal way. Although the muscles are in a state of flaccid paralysis, yet there is not that marked condition of hypotonia—*i.e.* loss of tone—seen in amyotonia congenita, and the legs and arms of the child cannot be placed in the abnormal positions which are so readily produced in the latter condition. The sphincters are normal.

Oppenheim's disease.—This condition is characterized by smallness,

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FIG. 451–454.—PROGRESSIVE SPINAL MUSCULAR ATROPHY: A SERIES OF PHOTOGRAPHS OF A CHILD, SHOWING PROGRESSIVE WASTING AND WEAKNESS OF MUSCLES.

The disease started when the child was twelve months old. The first photograph was taken when the child was three years old, the second when four years old, and the third and fourth when five years old (six months before death). The spinal cord showed the characteristic atrophy of the anterior horn cells. (Bruce and Thomson's case.)

FIG. 451.

FIG. 452.

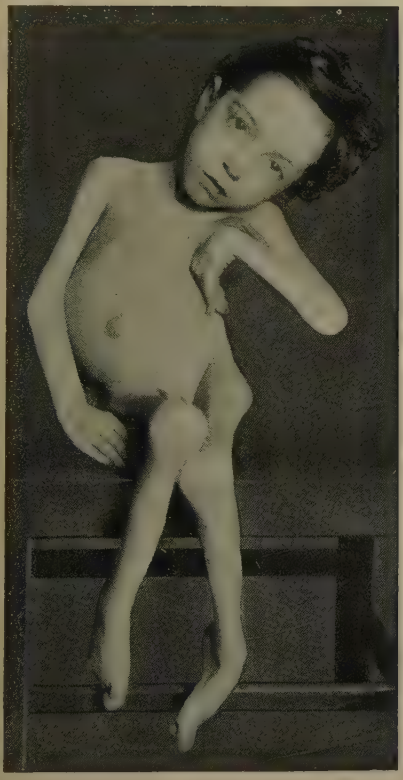

FIG. 453.

FIG. 454.

lack of power and loss of tone in all the muscles of the body, without localized atrophy of individual muscles or groups of muscles.

The muscular weakness is usually noticed from birth. In eighteen out of twenty-five cases collected by Collier and Wilson, the paralysis was observed at the time of birth. There is a tendency for a gradual improvement to occur, and, as development takes place, the child may learn to sit up and possibly to stand with support. The familial incidence, referred to as common in Werdnig-Hoffmann's disease, is seldom present in amyotonia congenita.

The most striking feature is the extreme hypotonicity of the muscles, which allows of the limbs being placed in contortionist positions; the arms folded behind the back, or the heels placed behind the ears. The feet and hands often appear unduly long, and, owing to the flexibility of the muscles, can be bent to unusual angles on the legs and forearms.

FIG. 455.—MYOPATHY: SIMPLE ATROPHIC TYPE, SHOWING THE "FOLDED-UP" POSITION CAPABLE OF BEING ASSUMED OWING TO THE MARKED HYPOTONIA OF MUSCLES.

All movements can be performed, but in a feeble manner, and those against gravity are conspicuously weak. The head appears too heavy for the neck and rolls about if unsupported. In many cases, the neck has an abnormally fragile thin appearance from smallness of its muscles, and the sterno-mastoids may appear to be absent unless the head is rotated laterally from side to side to bring these muscles into prominence. The movements of the face are usually perfectly good, but some cases have been described in which the face and tongue have been affected. The diaphragm is not involved and the ocular muscles are unaffected.

The deep reflexes are much diminished or abolished, but may make an appearance as the child grows older. Cutaneous sensation is usually perfect and the control of the sphincters is normal. There is no intellectual weakness. In the later stages of the disease, some contraction of the flexors of the legs and spinal deformity may occur.

These children frequently adopt strange manœuvres for getting about; sometimes they roll round on the long axis of the body in order to cross the floor, or other children assume the frog position. If the children

are placed on the floor and asked to get up, they are frequently unable to do so without the aid of a chair; sometimes they go through the manœuvres adopted by the pseudo-hypertrophic, sometimes they can raise the pelvis, but are unable to erect the trunk on the thighs.

THE TWO TYPES OF INFANTILE MUSCULAR ATROPHY CONTRASTED.—The time at which the muscular weakness is first noticed in the Oppenheim type of infantile muscular atrophy is usually at birth, but in some cases it is delayed until some weeks or months after birth. Contrariwise, in the Werdnig-Hoffmann type of muscular atrophy, the paralysis commonly develops some weeks or months after birth, but in other cases the disease would seem to have been present from birth.

A familial tendency is noticeable in the Werdnig-Hoffmann disease, but more than one member of a family may be affected by amyotonia

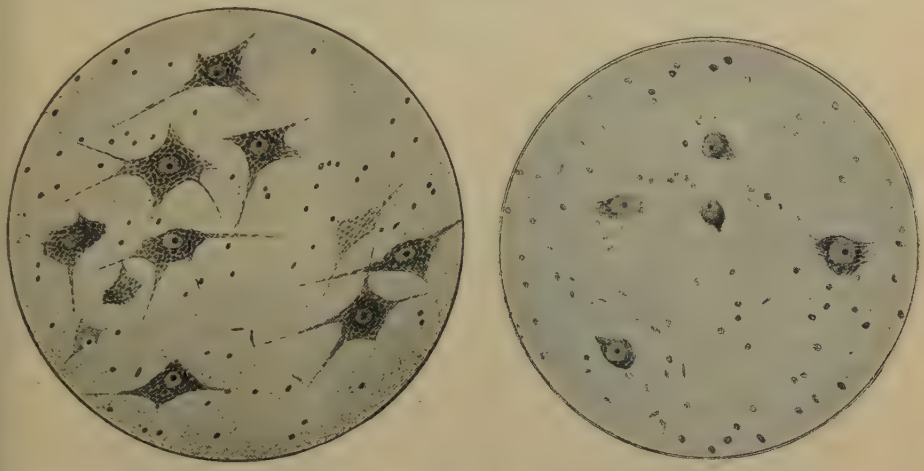

FIG. 456.—PROGRESSIVE SPINAL MUSCULAR ATROPHY: CELLS FROM THE ANTERIOR HORNS OF LUMBAR REGION OF THE SPINAL CORD, SHOWING ATROPHY, WITH LOSS OF CHROMATIN SUBSTANCE.

Compare the normal cells on the left with those on the right from the same segment of the cord and under the same magnification.

congenita. Moreover, instances are on record of one child of a family being clinically an example of progressive spinal muscular atrophy, while another child has presented all the features associated with Oppenheim's disease. Pearce describes an instance of twins, both of which were weak at birth. One twin gradually improved, while the condition of the other steadily became worse.

In contrast to the gradual but limited improvement which usually takes place in amyotonia congenita, most cases of progressive spinal muscular atrophy succumb in a short space of time, but remission of the symptoms has been noticed and death in some instances has not occurred until after several years have elapsed. It is doubtful if patients with amyotonia congenita ever make a complete recovery, for it seems improbable that the affected neurons should ever reach a state of normal physiological integrity.

In both conditions the strength of the faradic current necessary to produce contraction of the muscles is much increased, and in Werdnig-Hoffmann's disease no contraction may be obtained. The response of the muscles to the galvanic current may also be absent, but in amyotonia congenita there is generally a brisk contraction.

Keeping in mind that the actual cause of the disease in each case is entirely unknown, it is scarcely possible to form a definite opinion as to what relationship, if any, the two conditions bear one another. The extent of knowledge is limited to knowing that the morbid factors responsible for both the clinical conditions begin to operate in intra-

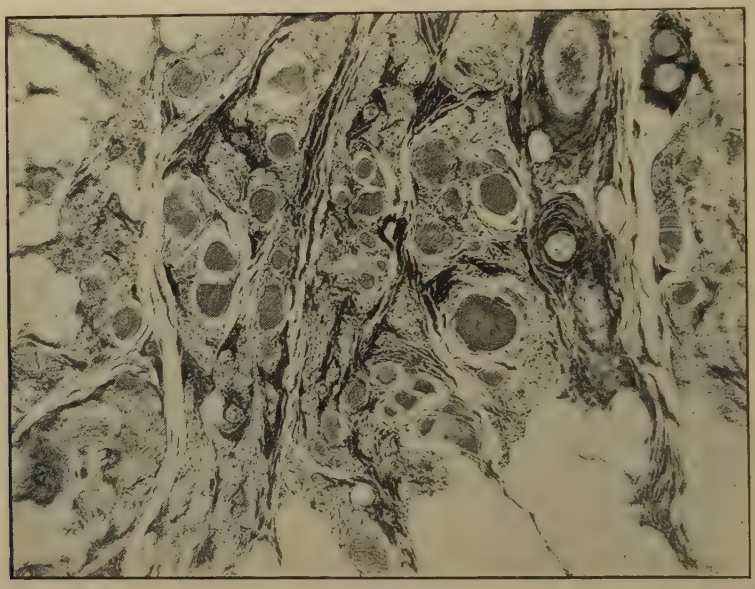

FIG. 457.—TRANSVERSE SECTION OF BICEPS FEMORIS MUSCLE, FROM CHILD SUFFERING FROM PROGRESSIVE SPINAL MUSCULAR ATROPHY OF INFANTS. (WERDNIG-HOFFMANN.)

Note the extreme variation in the size of the muscle fibre. The larger fibres are about normal size (*Brain*, 1912, **35**, 38).

uterine life, or within the first year after birth, and give rise to identical pathological changes in each instance.

Pathology.—The anatomical changes in the Werdnig-Hoffmann type of infantile muscular atrophy have been described by Werdnig-Hoffmann, Bruce and Thomson, Beevor, Armand-Delille and Bordet, Bruns, Holmes, Stanley, Parsons, and Batten. The cases of amyotonia congenita with atrophy have been collected by Greenfield and Stern and the results of histological investigation given in tabular form. As the pathological picture in these two conditions is exactly similar, the following description will suffice for both.

To the naked eye, the only change visible is the atrophy of the anterior roots of the spinal cord and the paleness and smallness of the muscles.

The principal changes that may be seen under the microscope are an atrophy, degeneration and reduction in the number of the ventral horn cells of the spinal cord; atrophy of the ventral roots; thinness of the peripheral nerves and atrophic changes in the muscles. There is demyelination of many of the fibres of the ventral roots and the number of thin, poorly myelinated fibres in the peripheral nerves is usually conspicuous (Greenfield and Stern). The cells of the hypoglossal nucleus may show degenerative changes and be reduced in number.

In the muscles, hypertrophy of individual fibres is not commonly seen and the general appearance suggests an atrophy secondary to some spinal change. The absence of intermuscular fibrosis, as compared to that which occurs in cases of myopathy, is a striking feature.

Diagnosis.—An infant, who in the first few weeks or months of life gradually develops a flaccid paralysis of the extremities, is probably the subject of a progressive spinal muscular atrophy.

An infant, who at the time of birth is said to have had a complete flaccid paralysis of both arms, legs and trunk, is probably the subject of an extensive injury to the spinal cord in the cervical region. The cerebro-spinal fluid may be blood-stained and sensation will be impaired below the level of the lesion. Again, in an early case in which the paralysis has not yet become extensive, a syphilitic epiphysitis must be borne in mind; for this condition frequently gives rise to a flaccid paralysis of one or both arms. The Wassermann reaction will decide the diagnosis.

Another condition which may closely resemble the spinal atrophy of infants is a flaccid paralysis of the limbs with absent knee-jerks, met with in certain forms of mental defect. Such cases, which are probably due to some general defect in development of the nervous system, should not be classed with the spinal atrophies.

The conditions with which amyotonia congenita are most easily confused are rickets—acrobatic rickets—and debilitated states following on an illness. Evidence of skeletal alterations due to rickets, or a history of a preceding illness, will help to distinguish these conditions. The muscular weakness in amyotonia is in most cases present from birth.

Prognosis.—Cases conforming to the Werdnig-Hoffmann type of infantile muscular atrophy become progressively weaker and death from respiratory failure takes place usually before the end of the second year. In Oppenheim's disease, slight improvement often appears to occur as the child grows, but it remains thin, weak, and often develops contractures at knee and ankle. It is doubtful if many survive into adult life. Resistance to respiratory complaints is extremely poor.

Treatment.—Fresh dried whole wheat germ, $\frac{1}{2}$ ounce daily, can be given a trial. There is little reason, however, to suppose there is any relationship between the neurological signs obtained in rats fed on a vitamin E-free diet and the infantile muscular atrophies beginning at or before birth and so often familial in incidence. In the myatonic type massage and measures to prevent contractures occurring are essential.

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NEURITIC TYPE OF PROGRESSIVE MUSCULAR ATROPHY

(Peroneal type—charcot-marie-tooth)

Introduction.—This form of progressive muscular atrophy lies midway between the myopathic and myelopathic affections. In its

Fig. 458.—Photograph of a Boy, aged Seven, suffering from the Peroneal Type of Muscular Atrophy.

Note the wasting of the legs, below the knees, the foot-drop and inversion of the feet, and also the wasting of the small muscles of the hands.

clinical aspects it is closely allied to the myopathies, but anatomically a definite change in the spinal cord has been established. The characteristic features of this affection are a slow, progressive muscular atrophy, with weakness, starting usually in the peroneal and anterior tibial muscles,

spreading gradually to the other muscles, so that all those below the knee are wasted, whereas the thighs remain in moderately good condition. Following the atrophy of the legs, the small muscles of the hands and forearms may begin to waste. There may be some alteration of sensation over the periphery of the legs and vaso-motor disturbances are common.

Ætiology. Age.—The disease usually starts during the first decade, but may appear in the second or third decade of life.

Heredity.—It is transmitted by both males and females and both sexes are attacked. But in the family reported by Herringham males only were affected, although the disease was transmitted by the females, following closely the hereditary features noticed in the transmission of colour-blindness. In a considerable number of cases no evidence of heredity can be obtained. In some instances the onset has directly followed measles (Ormerod, Batten).

Symptomatology.—The disease starts in the lower extremity, with weakness and wasting of the peronei, which give rise to foot-drop and inversion of the foot, so that the child walks on the outer side of it. The atrophy progresses and involves all the muscles below the knee, but the patient is usually well able to get about, as the muscles of the thigh remain in good condition. The distribution of the atrophy gives the leg a curious bottle-shaped appearance, the lower portion of the leg representing the neck of the bottle.

Charcot pointed out that it is the distal portion of the muscle which is first affected. Fibrillary tremors have been observed. In association with the atrophy of the muscles there is some loss of tactile sensation, and loss of muscular sense has also been observed. The muscles and nerve trunks are not tender. Vasomotor disturbances are sometimes present, generally in the form of cyanosis, but sometimes there is a marble-white appearance of the extremities. The muscles lose the power of contracting to mechanical stimuli, and there is a diminished reaction to faradism and galvanism, but a true reaction of degeneration is seldom observed. The condition is nearly always symmetrical, although exceptions to this rule occur (Herringham, Ormerod).

The ankle-jerks are usually lost at an early period and it is difficult to obtain a plantar response. The knee-jerks remain active and there is little tendency for them to disappear, as the vastus internus muscle remains in good condition. The sphincters and trunk muscles are not affected. After the atrophy of the legs has been present from one to four years, the disease may become arrested, or wasting of the small muscles of the hand may occur. This gives rise to a typical claw-hand, the two terminal phalanges being flexed. The disease may affect the extensors and flexors of the wrist. The atrophy, as in the legs, falls on the most distal muscles and the distal portion of the muscles. The degree of incapacity to which this affection gives rise varies greatly. Some patients are able to follow their usual occupation for years. Walking is their main difficulty and this they surmount by riding a bicycle, which they are able to do perfectly well. The mental condition is good.

Pathology.—There is some confusion with regard to the pathology, owing to the fact that several different conditions have been included under the neuritic muscular atrophy of Charcot-Marie-Tooth. Sainton carefully reviewed the subject and excluded many of the doubtful cases. In the case recorded by him the following changes were found. The cord showed sclerosis of the posterior columns, especially of the columns of Burdach; slight degeneration of both pyramidal tracts; alteration of the cells of Clarke's column; and atrophy of the cells of the anterior horns. There was slight degeneration of the intra-muscular nerves, slight sclerosis of the nerves of the forearm and leg, this being well marked in the peroneal nerves only. The larger nerves, such as the sciatic, were normal. The muscular fibres were atrophied and in some cases had completely disappeared, connective tissue being substituted. Almost the same changes were found in Siemerling's case, the degeneration being most advanced in the postero-median columns and in the lumbar and lower dorsal regions of the cord. The change in the muscles was that of simple atrophy of the muscle fibres, and not such as is met with in the myopathies.

Diagnosis.—The diagnosis of a characteristic case is not difficult. The slow onset, the character of the weakness and wasting, the absence of pain and the symmetry of the affection, are the points on which most stress would be placed.

The muscular dystrophies, and especially the "distal" type, bear a strong resemblance to peroneal muscular atrophy, and, as Spiller has pointed out, it is sometimes impossible to arrive at a correct diagnosis from clinical examination alone.

Prognosis.—Though of a progressive nature, the disease may become arrested, or advance so slowly that many patients are able to pursue their ordinary work for years. The acute specific fevers accentuate the disease and sometimes call forth its first manifestation.

Treatment.—No treatment is known to have any effect in arresting the disease. Mechanical support for the drop-foot will often assist the patient considerably in walking.

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PARALYSIS OF THE CRANIAL NERVES

(Congenital, acquired, recurrent)

(1) **Congenital paralysis of the cranial nerves** is extremely rare. Instances of the paralysis of the third, fifth, sixth, seventh, ninth and twelfth cranial nerves have come under personal observation.

Paralysis of the *third nerve* may be hereditary as well as congenital. It is commonly bilateral, giving rise to a complete paralysis of the external muscles supplied by the nerve, and to a partial or complete

ptosis. It may be associated with a paralysis of the sixth nerve, so that there is a complete ophthalmoplegia externa. The pupils usually react to light, and vision is good. Bradburn has described congenital ophthalmoplegia in five generations of a family.

Congenital paralysis of the *sixth nerve* manifests itself by paralysis of the external rectus muscle and results in the patient being unable to move the eye in an outward direction. Such a paralysis may give rise to an internal squint.

Congenital and familial nystagmus is a rare condition. Nettleship (1909) collected 25 pedigrees. Some of these would appear to be due to diseases or defects of the retina, choroid, or optic nerve, but others cannot be attributed to such causes.

Paralysis of the *fifth nerve* occurs in association with that of other cranial nerves and manifests itself by weakness of the masseter and temporal muscles.

Congenital facial paralysis is more often bilateral than unilateral and occurs in association with cranial nerve defects. Improvement does not take place in the congenital type. A true facial paralysis of congenital origin is in all probability due to a defect in the development of the seventh nerve nucleus, partial or complete (Babonneuse and Heron). Bilateral facial weakness has been observed in infants from birth, giving rise to difficulty in sucking, absence of emotional expression on laughing or crying, except for flushing of the child's face, and may be the earliest expression of a myopathy which will assume a more definite type at a later age.

Both unilateral and bilateral affections of the nucleus of the *twelfth nerve* may be present from birth, giving rise to atrophy and loss of power on one or both sides of the tongue. The atrophic tongue is sometimes seen in association with a facial paralysis.

Nuclear defects, aplasia and the "infantile nuclear atrophy" of Mœbius, probably account for most of these congenital paralyses of cranial nerves.

(2) **Acquired paralysis of cranial nerves.**—Acquired paralysis of the *third nerve* may be caused by tumour, vascular lesions, birth injuries, meningitis, and tumours of the orbit, interfering with the function of the nerve at any point from its origin in the region of the corpora quadrigemina to its termination in the muscles of the eye. When some muscles supplied by the third nerve are paralysed, while others are unaffected, the lesion probably lies in the region of the nucleus. If the upward and downward movements of the eyes are paralysed while the lateral movements remain good, the lesion is almost certainly situated in the anterior portion of the nucleus. A slowly progressive opthalmoplegia suggests the probability of tumour. An infective paralysis of the third nerve is seen in diphtheritic paralysis, affecting accommodation in both eyes. Syphilitic ophthalmoplegia is rare in children.

The *sixth nerve* owing to its long course is most readily paralysed by pressure in any case of raised intracranial tension, whether from tumour, meningitis, or other cause. In association with mastoid disease, when

the inflammatory process has spread to the petrous portion of the temporal bone lateral to the sella turcica in the neighbourhood of the cavernous sinus, the sixth nerve may be paralysed, giving rise to an internal strabismus, thus constituting what is known as Gradenigo's sign.

No cranial nerve is so frequently affected as the *seventh*. This is chiefly due to its long course through a bony canal and its exposed position as it crosses the ascending ramus of the mandible. Facial paralysis present at birth is often due to the pressure of forceps and usually passes off rapidly, unless an actual rupture has occurred. In infants and children the common cause of facial paralysis is an infection of the middle ear. Other causes of facial paralysis are herpes of the geniculate ganglion, poliomyelitis, and inflammations unspecified of the nerve within the Fallopian canal—Bell's palsy. Tumours situated at the base of the brain at the pontocerebellar angle readily give rise to facial paralysis. With a nuclear and infranuclear form of paralysis, the upper as well as the lower parts of the face suffer, whereas with a supranuclear lesion the forehead is not affected and emotional movements are less impaired than voluntary.

Several cranial nerves are affected, usually bilaterally, in toxic polyneuritis (p. 1354).

(3) **Recurrent paralysis.**—The only nerve which may show a recurrent paralysis is the *third*. In attacks of "ophthalmoplegic migraine" the onset of the paralysis is attended with severe ipsolateral headache and marked constitutional symptoms. The paralysis of the muscles involved may pass off in a few days or weeks, but if similar attacks occur in quick succession without recovery in the intervening periods, some degree of paralysis may become permanent. The youngest age at which the writer has witnessed a case of ophthalmoplegic migraine was seven years. In some cases the condition is associated with congenital aneurysms of the basal cerebral vessels and in these subarachnoid hæmorrhage is liable to occur.

DIPHTHERITIC PARALYSIS

Introduction.—Unrecognized diphtheria, which has not been treated with antitoxin, is not infrequently followed by paralysis. The clinical features of such a paralysis form a definite symptom-complex which is not produced by any other toxin. The most severe cases of paralysis occur in nasal and faucial diphtheria.

Ætiology.—There is but one cause of diphtheritic paralysis and that is the presence of the Klebs-Loeffler bacillus. It is not necessarily the severest cases of diphtheria which are followed by paralysis. Sometimes it follows the mild cases. The toxin affects strong and feeble children alike. There is, however, a greater danger of cardiac failure following on a severe case of diphtheria than on a mild one. The majority of cases of diphtheritic paralysis, Rolleston states, occur between the ages of two and ten years.

Symptomatology.—The first symptom to appear is usually that of weakness of the palate, which gives rise to a nasal voice and to regurgitation of liquids through the nose. This symptom usually appears about ten to fourteen days after the onset of the diphtheria, but is delayed in some cases until between the sixth and eighth week after the sore throat. Next, ocular paralysis, usually limited to paralysis of accommodation, occurs about the fourth week. Most cases of diphtheritic paralysis are afebrile.

During the early stages of the disease the knee-jerks are present and in some cases are temporarily exaggerated, but by the fifth, sixth, or seventh week they are usually diminished or lost. Walshe states that the ankle-jerks tend to disappear before the knee-jerks. A diffuse paralysis, commonly symmetrical, of the muscles of the limbs and trunk, becomes manifest. There is usually no movement which the child cannot perform, but the power is feeble. The diaphragm may become paralysed and respiration is carried on by the intercostals and accessory muscles of respiration. Sensation is usually unimpaired, but both subjective sensations of pricking and aching, and objective diminution of sensation, are occasionally detected in the peripheral portions of the limbs. The amount of muscular wasting which occurs is usually slight, but in some cases it may be considerable and may leave a permanent weakness and atrophy of muscles.

The course of diphtheritic paralysis is subject to considerable variation. In some cases, the paralysis remains limited to the pharyngeal and ocular muscles, and, as these symptoms usually pass off in four to five weeks, recovery may be complete in six to eight weeks after the initial attack of diphtheria. The paralysis of the diaphragm does not usually last long. In other cases, with diffuse paralysis, recovery may take as long as six to eight months. The return of the knee-jerks is a good sign, but the knee-jerks may remain absent for months after recovery has been in other respects complete.

The condition of the heart in diphtheritic paralysis must always be carefully watched for any signs of cardiac failure. If there be irregularity of the action, equal spacing between the two sounds, or inaudibility of the first sound at the apex, then the greatest care must be exercised to prevent any strain on the cardiac muscle. Vomiting is an ominous sign of cardiac failure.

Pathology.—On microscopical examination, degenerative changes are found in the cranial nerve nuclei, the anterior horn cells of the spinal cord, and in the peripheral nerves. The muscles of the ventricles of the heart always show marked fatty degeneration of the fibres.

The earlier involvement of the cranial nerve nuclei, according to Walshe, is due to a direct transmission of the diphtheria toxin along the perineural channels from the area of membrane formation in the nasopharynx, while the later diffuse neuritis of the limbs is the result of a toxæmia.

Diagnosis.—Some cases of multiple peripheral neuritis, in which the cranial nerves are also affected, may closely resemble diphtheritic

paralysis. In these, the weakness of the limbs, the ocular and other cranial pareses arise more closely upon one another in point of time. The patient is often febrile, shows signs of a general constitutional disturbance, and an antecedent history of sore throat is not common. The absence, however, of the Klebs-Loeffler bacillus in examinations of the naso-pharyngeal secretions is of little significance, as in diphtheritic paralysis throat swabs are usually negative by the time the paralysis has appeared.

Treatment.—The treatment of a case of diphtheritic paralysis is almost entirely a matter of nursing. The child must be kept in a lying position and not allowed to be raised into the sitting position under any pretext. While there is paralysis of the palate, all liquid food should be thickened by the addition of starch in some form. The child should be fed with small quantities every three hours, and the greatest care must be exercised in feeding, so as to avoid choking. It may be necessary to resort to feeding by the nasal tube. Should vomiting occur, it is important to regulate the feeding by reducing the quantity given at any one time, and to increase the frequency. It is often advisable to give the food in a predigested form, *i.e.*, to peptonize the milk and convert the starch.

In the prevention of cardiac or respiratory failure, the hypodermic injection of $\frac{1}{200}$ grain of strychnine and $\frac{1}{200}$ grain of atropine, every four hours, is of value.

The administration of the anti-diphtheritic serum is useless after the paralysis has appeared.

POLYNEURITIS

(Acute toxic or febrile polyneuritis)

Introduction.—The occurrence of a symmetrical neuritis in childhood is a rare event. Many of the causes which may lead to a multiple neuritis in the adult are uncommon in childhood. Thus alcohol, lead, or arsenical poisoning are infrequent in children. Diphtheritic paralysis is described elsewhere. Symptoms resembling a polyneuritis have occurred in some epidemics of poliomyelitis. As a rare event, multiple neuritis follows one of the specific fevers, such as scarlet fever, measles, mumps, whooping cough.

There remains a group of cases, supposedly of virus causation, more common among adults than children in which the polyneuritis is associated with, or preceded by, a rise of temperature, drowsiness, and other constitutional disturbances, which symptoms are often attributed to tonsillitis, "influenza," or food poisoning. The condition usually occurs sporadically, but instances of one or more children in the same family having been affected have been observed. Such cases are referred to as *acute toxic* or *febrile polyneuritis*. The cranial nerves are commonly involved as well as those of the limbs, and in some instances have been almost solely affected—*polyneuritis cranialis*.

Symptomatology.—Symptoms of a constitutional disturbance, fever, headache, drowsiness, aching pains in the limbs, either precede or occur synchronously with the onset of muscular weakness. The neuritic symptoms develop quickly. Of the cranial nerves involved there is usually bilateral facial weakness, sometimes palatal weakness and ocular palsies, internal, paralysis of accommodation, or external, ophthalmoplegia. All four limbs are affected together, or the legs before the arms, and the large proximal muscle groups may be affected as badly, if not more so, than the peripheral. The tendon reflexes are lost, and drop-foot and drop-wrist occur. Trembling of the limbs on voluntary exertion is observed. Tenderness of the muscles, or along the nerves, is usually present and a slight degree of sensory impairment in the distal parts of the limbs.

The cerebro-spinal fluid in toxic polyneuritis may be normal, or show a considerable increase of protein content, often with a xanthochromic colour, and a small increase of cells, chiefly lymphocytes.

Recovery occurs in nearly all cases in a period of one or two weeks to several months. Second attacks, or *recurrent polyneuritis*, are very uncommon in children.

Pathology.—There is evidence of a diffuse inflammation of peripheral neurons more obvious in the nerve fibres than in the ganglion cells of the spinal cord and brain-stem.

Treatment.—Treatment consists of rest and massage, and splints are needed to prevent the occurrence of deformities.

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POLYNEURITIS WITH UVEO-PAROTITIS

Introduction.—The syndrome of enlargement of the parotid glands and inflammation of the uveal tract, usually manifested as irido-cyclitis, may be accompanied by polyneuritis. The form of neuritis most commonly present is a facial palsy, either unilateral or bilateral. The facial weakness sometimes precedes the uveo-parotitic signs, but more often follows them. A more generalized polyneuritis may occur with loss of tendon jerks, weakness of the legs, subjective sensory disturbance, and palatal weakness. A slight elevation of temperature and other symptoms of a mild constitutional type are present in some cases in the early stage of the disease, which tends to run a chronic course and usually ends in spontaneous recovery. Children, as well as adults, are affected, but more often in the second than in the first decade.

Ætiology.—In an analysis of forty-three cases of inflammation of the parotids and uveal tracts, Garland and Thompson used the title

of uveo-parotid tuberculosis, but the condition is probably a form of Boeck's sarcoidosis. Polyneuritis is not a constant feature of the syndrome.

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PROGRESSIVE HYPERTROPHIC POLYNEURITIS

Synonyms.—Déjerine and Sottas' disease.

Introduction.—This uncommon form of neuritis is characterized by thickening of the peripheral nerves and wasting of the muscles at the periphery of the limbs. The disease is sometimes familial and hereditary. Clinically, in some cases it resembles the neuritic or peroneal type of progressive muscular atrophy, in others with absent tendon jerks and an extensor plantar response a similarity to the group of the familial ataxias has been noticed. The onset of symptoms may be before the tenth year, but is usually later, in adult life.

Symptomatology.—A slowly progressive muscular atrophy, usually starting in the feet before the hands are affected, spreads up the leg and the arm. Fibrillary twitching of the muscles may be observed. Pes cavus and claw-hand develop. In some cases sensation is unimpaired, in others sensory disturbances of a glove and stocking type are present in the limbs. The tendon jerks are lost, and an extensor plantar response may be obtained. The characteristic enlargement of the peripheral nerves may be visible or palpable, but is not always conspicuous. Other symptoms which may be present are kypho-scoliosis, ataxy, nystagmus, and pupillary abnormalities.

Pathology.—The thickening of the peripheral nerves is due to an increase of the interstitial tissue, and there is also a proliferation of the cells of the sheaths of Schwann. A simple atrophy of the muscles is observed. Within the spinal cord a degeneration of the posterior columns is frequently seen.

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VON RECKLINGHAUSEN'S DISEASE

Synonyms.—Diffuse or generalized neurofibromatosis.

Introduction.—This disease was first described by von Recklinghausen in 1882, and is characterized by the presence of (1) multiple tumours of the skin (molluscum fibrosum); (2) subcutaneous tumours situated in the nerves, either plexiform or multiple (neurofibromata); (3) pigmentation of the skin. The tumours may be situated in any of the peripheral nerves, the cranial nerves, the nerve roots of the spinal

cord, or the sympathetic fibres, and in addition intracranial and spinal gliomas and meningiomas have been recorded.

Ætiology.—The disease is of congenital origin, sometimes hereditary and often familial, and is to be regarded as an example of the developmental tissue dysplasias. Epiloia is another and the two conditions have occurred in the same patient (Hall, 1940).

The tumours of the skin, pigmentation spots, and tumours of the nerves have all been observed at birth, or in early childhood. They often remain stationary for many years, or may at any time, and especially at puberty, take on active growth. Males and females are affected alike. In the seventy-seven cases collected by Alexis Thomson, twenty-eight presented symptoms at birth, or in early life.

Symptomatology.—*Pigmentation of the skin* is present in two forms: the first or punctiform variety, like dark brown freckles, and the second in which larger areas of skin are involved. The discoloration alone may be present at birth and followed later by the development of neurofibromatosis.

Cutaneous fibromata project from the surface of the skin, varying in size from a pin-head to large pedunculated masses of soft consistency. They may become numerous, but at birth it is unusual for more than a few to be present. They give rise to no pain except when in situations over which pressure is exerted.

Neurofibromatosis. Solitary or plexiform swellings of all sizes can be felt in the connective tissue along the course of the cutaneous nerves, or in the brachial, lumbar or sacral plexuses. They are usually insensitive and rarely give rise to anæsthesia, or to actual paralysis of muscles.

When the tumours are situated on the spinal roots, or on the cranial nerves, they give rise to the symptoms of intracranial or spinal tumour. The eighth or acoustic nerve is most often affected, and the growth may be unilateral or bilateral (p. 1263).

The optic nerves, chiasma and optic tracts, actually outgrowths of the brain, may be involved in a dense gliomatosis slowly or rapidly producing blindness, and usually in association with a glioma elsewhere in the brain.

In two cases seen at Great Ormond Street, one was that of a girl of 5½ years with symptoms of cerebral tumour and amaurosis. There was gliomatosis of the intraorbital portions of both optic nerves, the chiasma and tuber cinereum and a large cystic glioma of the right cerebral hemisphere. She presented also a patch of pigmentation and a fibroma of the skin. In the second case, a boy of one year, six months, developed signs of rapidly increasing intracranial pressure, prominence of the eyes, squint and rapid failure of vision. Post mortem, both optic nerves as they left the chiasma were greatly thickened and hard, whilst the chiasma and interpeduncular space were involved in a soft gelatinous mass proved to be a glioma.

Shapland and Greenfield describe a case of neurofibromatosis with involvement of the optic nerve, and gliomata in the cord and cerebrum.

Ganglio-neuromas, which are characterized by the presence of medullated and non-medullated nerve fibres and ganglion cells, arise more frequently in connection with the sympathetic nervous system and

adrenal medulla than the peripheral nerves. Their situation is commonly in the abdomen, thorax, or in the cervical region. When growing from the fibres of the spinal nerve roots, the tumour may be partially intravertebral causing signs of compression of the cord, and partially extrapleural or extraperitoneal. Erosion of one or more ribs due to pressure of the extravertebral portion of the growth may be visible on radiography.

Pathology.—Neurofibromata are caused by an overgrowth of the endo-, peri-, and epi-neurium, and of the sheaths of Schwann or neurolemma. The ganglio-neuroma with actual formation of nerve fibres and ganglion cells is a *true neuroma.*

Treatment.—Except in the case of a solitary eighth nerve tumour, or of a ganglioneuroma, it is important to avoid operation, as that is attended either by the production of paralysis from nerve severance, or by the stimulation into actual growth of the tumours. In general treatment, arsenic and iodides appear to have beneficial effect.

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BIRTH INJURY TO THE BRACHIAL PLEXUS

Introduction.—Injury to the nerves of the brachial plexus at birth occurs both in normal and abnormal presentations, but there is no doubt that traction exerted on the arms, or forcible flexion of the head to liberate the aftercoming arm, are the most common causes of brachial plexus paralysis. The injury may involve the upper or lower portion of the brachial plexus, or sometimes both portions may be involved. When the upper portion is damaged, a paralysis of the deltoid, supra- and infraspinati, biceps and supinator longus results. Such a paralysis is often designated an "Erb's paralysis," since he first described it. When the lower portion of the plexus is involved, the muscles of the hand and flexors of the wrist are principally affected and such cases are often designated "Klumpke's paralysis," since she first described this form.

Symptomatology.—Loss of power is noticed in the affected arm immediately or soon after birth. The limb usually hangs flaccid by the side and movements are only made with the forearm and fingers. After the first few days, the arm is rotated inwards and the palm of the hand turns so as to face outward, and, if the condition persists, the contraction of the pectoral muscle renders this position more or less permanent. The arm is usually extended and cannot be rapidly flexed at the elbow. In cases in which the lower portion of the plexus is involved, it is the hand and forearm muscles which are affected, while the upper arm remains normal.

Almost every degree of paralysis may be seen—from cases in which

there is only weakness of the deltoid to those in which there is a complete paralysis of all the muscles of the arm and shoulder.

It is a striking fact that in most cases sensation is little if at all affected. In lesions involving the eighth cervical and first dorsal root, there may be evidence of paralysis of the sympathetic on the side of the lesion—*i.e.*, slight ptosis, a small pupil and palpebral fissure.

Pathology.—The condition is due to traction on, rupture of, or hæmorrhage into, the nerve trunks of the brachial plexus. The rupture usually occurs after the junction of the fifth and sixth roots of the brachial plexus to form the upper cord. In some cases all the cords of the brachial plexus may be involved in fibrous tissue.

Diagnosis presents but little difficulty. Dislocation of the shoulder might give rise to a weakness of the arm, but this cause would be readily recognized. A paralysis of the arm from hemiplegia would be associated with weakness of the face and leg on the same side. A monoplegia of cerebral origin might give rise to some difficulty in diagnosis, but such a condition is very rare. Neither the absence of wasting, alteration of electrical reaction, nor rigidity, points of importance in older children, are of much service in infants. If the condition is seen some weeks after birth, an epiphysitis must be thought of; but epiphysitis commonly gives rise to a flaccid paralysis and the enlargement of the epiphysis will be evident, if not immediately, at any rate a few days after the paralysis is first noticed. It is impossible in an infant to differentiate a lesion in the spinal cord alone from one in which the brachial plexus and the spinal cord are simultaneously affected.

Fig. 459.—Erb's Birth Palsy. (From a photograph supplied by Sir Thomas Fairbank.)

Prognosis.—The prognosis in most cases is favourable. In those which recover rapidly, it is probable that traction has produced a physiological interruption, and after a few days or weeks complete recovery of function occurs.

In some few cases, recovery takes place after three to six months. In these, it is probable that there has been some rupture of fibres and regeneration has slowly taken place. In other cases, only partial recovery occurs. In such cases, matting round the brachial plexus is generally found. In yet other cases, no recovery takes place, and in these extensive injury of the plexus and spinal cord are found.

Treatment.—The slighter cases may be left to themselves to recover,

which they do in a few days or weeks. In all cases it is advisable to place the arm in the position of abduction and external rotation of the humerus and to keep it in this position either with plaster, or a properly adjusted splint. Massage, passive movements and electrical applications are of advantage a little later.

SCALENUS ANTICUS SYNDROME

The scalenus anticus syndrome consists of pain, paræsthesiæ, sensory impairment of ulnar distribution, and reduced volume of the radial pulse on the same side, due to compression of the subclavian artery and of the brachial plexus, especially of its lower roots seventh and eighth, in the angle formed by the outer border of the scalenus anticus at its insertion into the scalene tubercle of the first rib. A supernumerary or cervical rib, or an enlarged seventh transverse process, may or may not be present. In persons with markedly sloping or low position of the shoulders and an apparently long neck, the tendency to compression of the seventh and eighth cervical roots in the angle formed by the scalene muscle is increased, and, as the nerve supply of the muscle is in part derived from the seventh and eighth roots, spasm is aggravated and a vicious circle set up. In such subjects, by focusing the X-rays at the level of the first dorsal vertebra, the rœntgenogram will show the junction of the first rib with sternum to be at an unusually low level, opposite the fourth or fifth dorsal body.

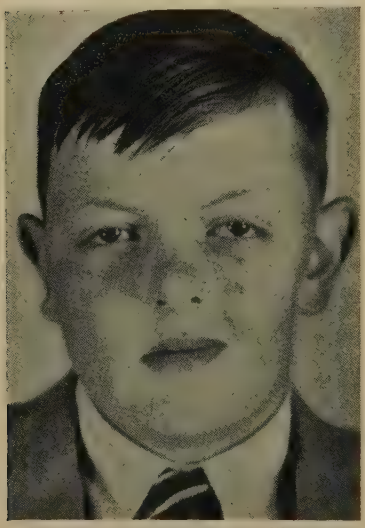

FIG. 460.—LEFT-SIDED FACIAL HEMIATROPHY.
(Dr. Donald Paterson's case.)

Adson and Coffey first drew attention to the relief obtained from the symptoms of cervical rib by section of the scalenus anticus. Donald and Morton report twenty-one cases of the syndrome, of which thirteen had no cervical rib. The age of patients is seldom below twenty years, and the youngest in the writers' experience was a girl of eleven, who had aching pains, pins and needles in the ulnar border of the right arm and hand, and a sensation of a weight pressing upon the shoulder, aggravated by carrying heavy objects, or raising the arm up and backwards during physical exercises at school.

In a young patient, treatment at first is by rest and an arm-sling, but if symptoms persist, section of the scalenus anticus will be required at a later age.

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HEMIATROPHY OF THE FACE

Hemiatrophy of the face is a rare condition occurring more often in childhood than in later life, characterized by progressive wasting of the skin, subcutaneous tissues, muscles and bones on one side of the face. There is no weakness of the muscles of the face and they react normally to electrical stimulation. There is no alteration of sensation. The wasting may become arrested, or spread to the other half of the face. The pathogenesis of the condition is unknown.

CHAPTER XXVIII

DISEASES OF MUSCLES

W. G. WYLLIE

CONGENITAL DEFECTS OF MUSCLES

Introduction.—Children are from time to time seen in whom there is congenital absence of a muscle, or part of a muscle. The condition is not associated with any form of progressive weakness and frequently does not give rise to any disability. The muscle which is most frequently absent

FIG. 461.—CONGENITAL ABSENCE OF MUSCLES OF THE ABDOMINAL WALL: PHOTOGRAPH SHOWING THE FURROWS IN THE ABDOMINAL WALL AND THE DEFORMITY OF THE THORAX. (GARROD AND DAVIES.)

is the lower portion of the pectoralis major. Bing collected 102 cases in which the trapezius was absent, and sixteen in which the quadriceps was absent. The absence of the lower portion of the pectoral is shown by asking the child to press the hands together while the elbows are abducted from the sides. Instead of the lower border of the muscle running in an oblique

line downwards, it runs transversely. This portion of the pectoral muscle may be absent on both sides; it must, however, be remembered that bilateral absence of the lower part of the pectoral is a characteristic feature in many cases of pseudo-hypertrophic paralysis.

The trapezius, serratus, quadriceps, are the muscles which, after the pectoralis, are most commonly absent.

Congenital absence of the abdominal muscles is one of the most interesting of these malformations. Records of 34 cases with partial or complete absence were collected by Housden, all being males, where the sex was stated, except one. In most, death occurs in early infancy, usually due to pulmonary complications owing to the difficulty in coughing. Associated abnormalities are often present, undescended testes, inguinal hernia, talipes, idiopathic dilatation of the colon, spina bifida occulta. In 23 of the 34 cases the bladder was said to be grossly enlarged, and in many of the autopsies found to be hypertrophied, often with associated dilatation and kinking of the ureters, and in a few with hydronephrosis. In this respect Hall considered that the defective development of the abdominal muscles in the embryo deprives the bladder of one of the influences whereby normally it is caused to descend within the abdomen. Secondarily, the enlarged bladder and ureters prevent descent of the testes.

The absence of the abdominal muscles give the abdomen a strange appearance; the whole surface of the skin is wrinkled, the longitudinal furrows being deepest, the abdominal wall feels thin and flabby, and the infant is unable to make any loud cry, or forced expiratory effort.

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DISEASES OF MUSCLE OF INFLAMMATORY ORIGIN

(1) **Myositis ossificans progressiva** signifies a condition in which there is a tendency for several muscles of the body to undergo ossification. It is a condition of early childhood or the period of growth and affects not only the muscles but tendons, ligaments, fasciæ and aponeuroses and is characterized by the development in them of masses of bone or areas of calcification. The number of recorded cases in England is about twenty-five, males being more often affected than females. It does not in itself tend to shorten life and may persist for many years; some patients have been afflicted with the condition for over forty years. Garrod observed the condition in a child of five months.

Ætiology.—The cause of the abnormal calcium metabolism has not been explained. Injury will not account for the generalized ossification which occurs. Mair states that the formation of new bone is not intra- but inter-muscular, and prefers the title of *fibrositis ossificans progressiva*

as the muscle fibres only secondarily become compressed, atrophied and disappear. He considers that the interstitial connective tissue undergoes replacement by a loose embryonic structure which is transformed into a cartilaginous ground-substance, in which the formation of true bone takes place. Bony outgrowths may also develop in the proximal joints of the limbs and on the vertebræ, and congenital abnormalities may be present, especially symmetrical deformities of the thumbs and great toes which are unduly short from absence of a proximal phalanx, or synostosis of shortened phalanges.

Symptomatology.—The first symptom is usually a local swelling on

Fig. 462.—Myositis Ossificans: Bony Nodules on the Back, Neck, and Iliac Crest. The feet show Microdactyly. (Sympson.)

the back, which is often attributed to injury. The swelling is situated in the muscles, is firm in consistency, sometimes painful and the onset may be accompanied by fever. There is often more or less œdema round the swelling, but the skin is not involved. After a few days the swelling tends to subside, leaving a hardness in the muscles which may eventually become bone.

Garrod, who had the opportunity of watching carefully the development and course of these swellings in a child under his care, says that they were of various sizes; they were most numerous on the back, but were also situated on the front of the chest, or on the limbs. The swellings formed round or oval bosses, very firm and elastic and with sharply defined margins; they were attached to the deeper tissues and the skin was freely

movable over them. They were not tender. From the base of some of the more defined swellings slender processes could be traced for some distance from the main boss. Swellings of a second kind appeared as diffuse thickenings of the soft parts, with indefinite outlines and over these the skin was not movable. Some of the masses underwent fission, a single boss becoming converted into two distinct bosses, connected by an area of diffuse swelling. These swellings might last nineteen to thirty-seven days and then completely disappear. After some weeks fresh attacks occurred, with further swellings in the muscles. Some of these did not subside and left a residual hardness which eventually became bone. In the initial stages of the disease, the bony tumours are at first small and multiple. They gradually enlarge, coalesce and form long bony masses of irregular shapes. These masses may be independent of bone, but, as the disease progresses, they generally become attached to bone and give rise to a great limitation of movement. Whenever a bony growth is formed, it never disappears.

The disease may affect any part of the body, but usually begins in the muscles of the neck and back. It advances slowly ; the shoulder-blades become fixed to the thorax, the neck becomes rigid, and finally the limbs, the masseters and temporal muscles become so fixed that the patient cannot eat. Such an advanced condition is rarely, if ever, seen in childhood.

Diagnosis. —The condition must not be confused with multiple exostoses, which is a familial and hereditary disease.

Treatment.—No means has been found of arresting the disease.

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(2) **Myositis fibrosa** is a rare condition in which a slow and progressive fibrous infiltration of the muscles occurs, similar to that found in myositis ossificans but without ossification and commencing in the lower limbs. The disease appears in childhood or early adult life and affects males more often than females.

Symptomatology.—First the muscles of the lower limbs are affected, with a gradual involvement of the muscles of the back and neck, the intercostals and abdominal muscles, and the sternomastoids. The overlying skin may be glazed and slightly œdematous.

The following case of a boy, aged six years, illustrates the leading features of the disease as well as the pathological condition.

The boy was well up till nine months old. His mother then noticed that his back was growing out and the legs were drawn up. The condition slowly progressed, so that the child became more and more bent up. When six years old, he could sit up in bed with the legs flexed, the back curved and the head bent forward on the chest, the face turned to the left owing to the contraction of the right sterno-mastoid. The spine was flexed in a curved condition and could not be straightened. The abdominal muscles were extremely hard and

contracted. The arms were fixed so that they could not be extended or adducted. Any attempt to move the limbs resulted in the moving of the body as a whole. The boy was rigidly fixed in a flexed position, unable to move. The great toe was shorter than the second, third and fourth toes (fig. 463).

Pathology.—The condition depends entirely on a change in the muscles, no change being present in the central or peripheral nervous system. The muscles when removed from the body are hard and firm, and when cut across are found to consist of a tissue which grates under the

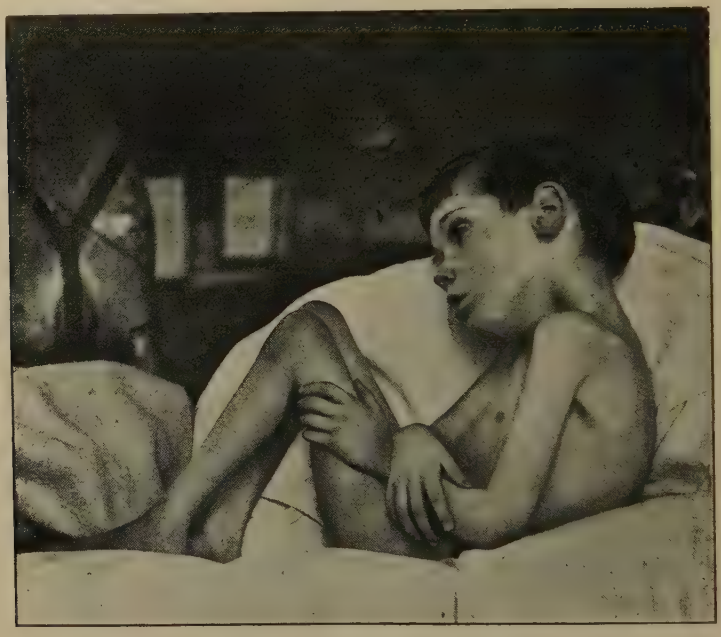

Fig. 463.—Myositis Fibrosa.

Note the curvature of the back, the flexion of the neck and limbs. The child lay constantly in this position, and any attempt at passive movement only resulted in movement of the child as a whole.

knife and appears hard and white on section. In less affected portions the muscle tissues appear as reddish-yellow points on a white ground. Microscopical examination shows a mass of the interstitial tissue between the muscle fibres, which have in part undergone granular degeneration, in part simple atrophy. In the most severely affected portions, the muscles are composed entirely of tendinous tissue.

Diagnosis.—The clinical resemblance to myositis ossificans is sometimes close, and it is only the complete absence of any evidence of bony formation within the muscle, as shown by X-ray examination, that justifies the diagnosis of myositis fibrosa.

Prognosis.—The disease is generally slowly progressive. Some cases have been reported in which recovery has taken place.

TREATMENT.—Massage, passive movements, hot-air baths and electricity should be tried. Recovery has been reported after this line of treatment.

REFERENCE

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(3) **Dermato-myositis or polymyositis.** The disease is an inflammatory condition of the skin, subcutaneous tissue and muscles, often starting acutely but tending to run a chronic course. The patient becomes bed-ridden from restriction of movement of the limbs and spine, and in a typical case the dusky red erythema of the supraorbicular region, the red atrophic skin over joints, especially the phalangeal and knee-joints,

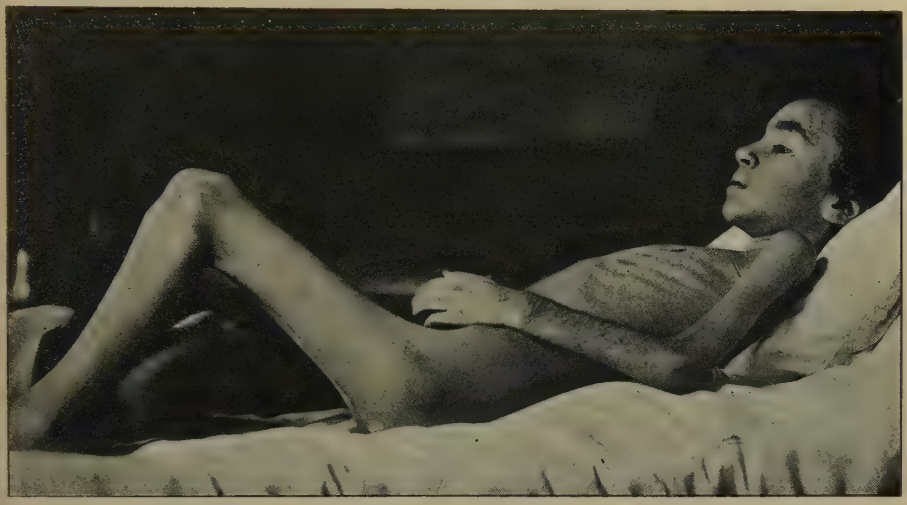

FIG. 464.—DERMATO-MYOSITIS: PHOTOGRAPH OF GIRL AGED NINE YEARS, SHOWING THE WASTED CONDITION OF MUSCLES AND THE GREATEST EXTENT TO WHICH THE ARMS AND LEGS COULD BE EXTENDED.

and the erythematous swollen appearance of the skin of the forehead, across the nose and cheeks and over the affected muscles elsewhere in the body are characteristic.

ÆTIOLOGY.—The cause of the inflammatory changes is unknown. The age of onset is any time between three and seventy years; most cases occur in adult life. In Steiner's record of twenty-eight cases, seventeen were fatal. Many die within two years from the onset, whilst a gradual recovery has occurred in a few cases.

An upset of muscle metabolism was confirmed by Bonham-Carter in two cases, in which the creatine output was found to be in excess of the creatinine, which is the reverse of normal. In the active stages of the disease the erythrocyte sedimentation rate is raised. An eosinophilia has been found, which must be remembered in differentiating the disease

from the muscular pain and rigidity which may occur in infection with trichinella spiralis. Langmead considers that a close relationship exists between scleroderma, dermato-myositis and the other forms of myositis.

Symptomatology.—The onset is often acute with general constitutional disturbance, mild pyrexia, progressive weakness of the limbs, vague pains followed by swelling and redness of the skin with pain and tenderness of the underlying muscles. The spleen is found to be enlarged in some cases.

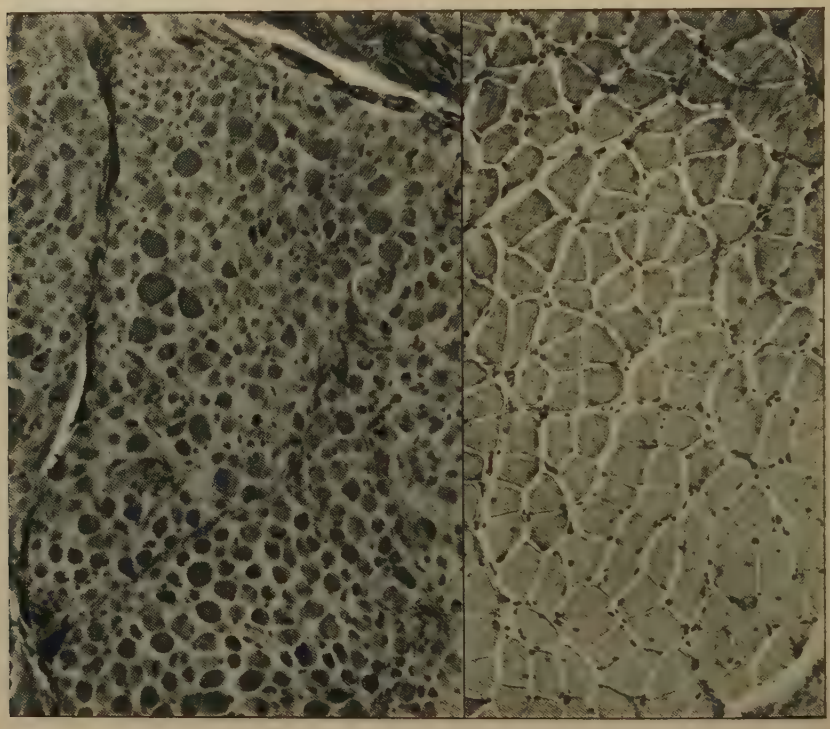

Fig. 465.—Dermato-Myositis: Section of Biceps Muscle of the Arm, showing Atrophy of the Muscle Fibres, which in Some Places have almost disappeared.

Note the small amount of interstitial tissue. A normal portion of the same muscle under the same magnification is seen on the right.

The swelling of the skin and muscles gradually subsides, but the subcutaneous tissue and muscles become brawny and indurated to the touch. Fresh attacks occur which eventually leave the skin and muscles in a more indurated state. There is no evidence of affection of the joints, but rigidity of the trunk and limbs develops with secondary contractures of the flexor tendons.

The skin lesions Steiner describes as resembling an erythema, a pseudo-erysipelas, an urticaria, or a roseola. Patchy erythema or squamos erythematous rashes cover the forehead, nose and cheeks, scalp, neck-trunk and limbs, especially over affected muscles, and in the latter stage,

gritty deposits of calcification both palpable and visible have appeared in the skin of the lower limbs. The skin over the knuckles, elbows, knees and ankles is thin and atrophic and has a red glazed appearance. A dusky-red erythema of the supra-orbicular areas is a striking feature of the cases in children.

Pathology.—The epidermis is thinned with disappearance of the papillary processes and round-celled infiltration and increased vascularity are visible. The superficial muscle fibres are more affected than the deep, showing atrophy and parenchymatous degeneration, increase of interstitial fibrous tissue, thickening and obliteration of vessel walls, and infiltration with lymphocytes, especially round the blood vessels.

Treatment.—Calcium and vitamin B have been tried without effect. In the more chronic stages, hot baths, massage and passive movements are useful, and if contractions are present extension and splints should be used to prevent deformity. Cortisone produces a remission which may last some time (Schlesinger, 1951), but further observations are necessary.

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THE MYOPATHIES

Muscular Dystrophy

Introduction.—Under this title are included those cases in which muscular weakness is the leading feature, such weakness being independent of a spinal lesion. The weakness may be attended by atrophy, hypertrophy, or pseudo-hypertrophy. Differences of the muscle-groups affected and of the age of onset have led to the recognition of several clinical types, but there is no essential pathological dissimilarity between them, and the myopathies form one composite class.

Ætiology.—The muscular dystrophies belong to the heredo-familial group of diseases. In genetics an association is seen to exist between the mode of inheritance and the clinical type. Transmission may be dominant, recessive, or sex-linked. Julia Bell finds that affected members from sex-linked families first show signs of their myopathy at about five years and usually die about the age of seventeen years, cases of dominant transmission often begin about nineteen and die at about fifty years, whereas recessive cases are intermediate. The pseudo-hypertrophic form is usually inherited as a sex-linked recessive, with transmission nearly always to males through apparently healthy females. A probable example of a pure dominant is the type ascribed by Barnes which occurred in five generations of a family, affecting males and females, and presenting four successive phases, hypertrophic, pseudo-hypertrophic, atrophic, and distal in the upper extremities.

The character of the muscular defect is unsolved. Alteration in the

metabolism of muscles such as a diminution of creatinine output and an increase of creatine are proportional to the extent of the muscular wasting and are entirely secondary effects of an obscure pathological process. It is to be remembered that in infancy and childhood there is to some extent a natural creatinuria.

The following varieties need description :

(1) Pseudo-hypertrophic type.
(2) Juvenile type of Erb.
(3) Facio-scapulo-humeral type of Landouzy-Déjerine.
(4) Distal type of Gowers.

FIG. 466. — MYOPATHY : PSEUDO - HYPERTROPHIC TYPE.

Typical case illustrating the relative large calves as compared to the thighs.

(With Dr. Collier's kind permission.)

(1) The pseudo-hypertrophic type.— This form of dystrophy is often familial. The age of onset is usually about the fourth to sixth year, but a history is frequently obtained that the boy was late in learning to walk and has never been able to climb stairs well.

SYMPTOMATOLOGY.—On inspection, enlargement of some muscles is seen, and wasting of others. The muscles commonly hypertrophied are the deltoids, infra-spinati, the glutei, the quadriceps and the calf muscles, and less often the triceps, the supra-spinati and the masseters. On palpation the hypertrophied muscles have a firm, tough consistency. The muscles commonly atrophied are the lower portion of the pectoralis major, the biceps, latissimus dorsi, and the thigh muscles.

The appearance of a child with well-marked pseudo-hypertrophy is striking. When he stands, there is marked lordosis of the lumbar spine, the shoulders are held far back, and the scapulae project. The large size of the buttocks often makes the lordosis appear more accentuated than it is in reality. The large size of the calves is in contrast to their weakness.

When walking, the child waddles. This form of gait has a double object : first, in order to get the centre of gravity directly over the hip-joint, and secondly, to get over the difficulty of raising the thigh. In walking, the trunk and head are usually held very erect; for unless this position is maintained, the balance of the child is liable to be upset, In sitting, the lordosis, which is present in standing, passes into a kyphosis, the back being bent according to the degree of weakness of the dorsal muscles.

If an attempt be made to lift up the child by placing the hands in the axillæ, the looseness of the shoulders is a striking feature. When placed

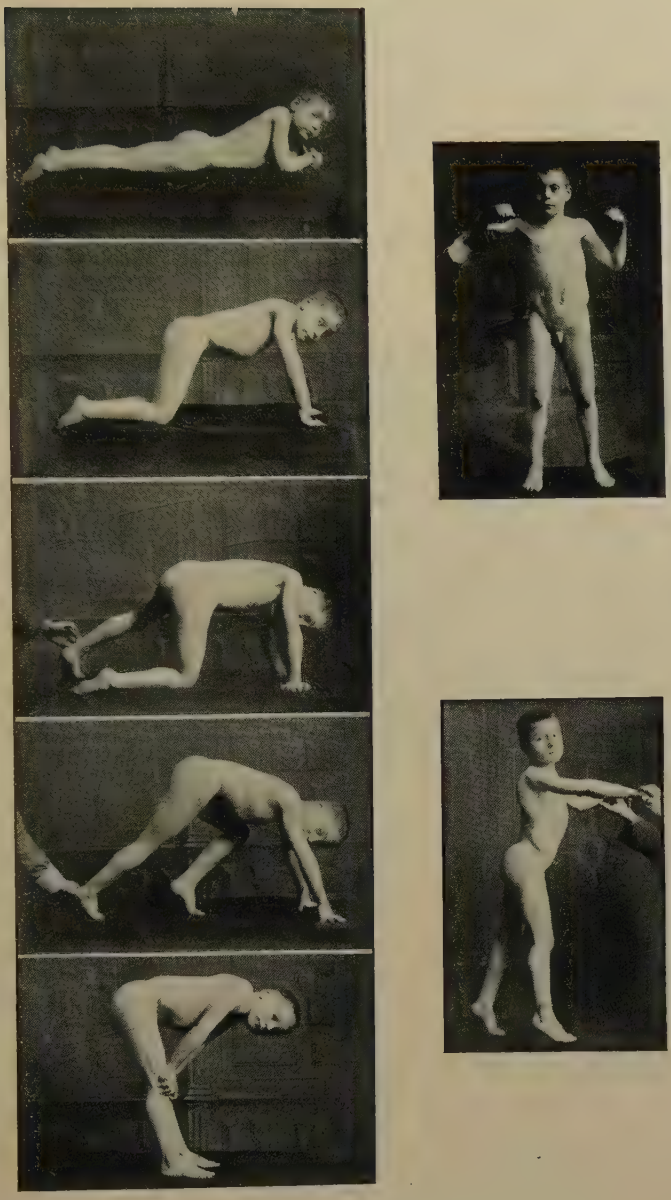

FIG. 467.—MYOPATHY : PSEUDO-HYPERTROPHIC TYPE.
A series of photographs illustrating the manœuvres adopted to attain the erect position.
(With Dr. Cox's kind permission.)

flat on his back on the ground and asked to rise, he goes through a definite series of movements to accomplish the act. The normal child, when asked to get up, sits up, flexes the legs under the trunk and rises into the erect position by the extension of the legs and thighs. The pseudo-hypertrophic child rolls upon his face on his long axis; he then draws his legs up under him, keeping his head on the ground. He now extends the legs, and, by working his hand backwards along the floor, brings the trunk to above the thighs. The trunk has now to be brought into the erect position; this is done by bringing the hands on to the legs and then on to the thighs and thus climbing up the legs, pushing the trunk into the erect position. With a little swing of the head the shoulders are thrown back and the trunk is balanced on the thighs, the lordosis appearing in the place of kyphosis.

FIG. 468.—MYOPATHY: ERB'S JUVENILE TYPE.

Note the winging of the scapulæ, due to weakness of the trapezius and serratus muscles; the other muscles of the body were normally developed.

In the earlier stages of the disease the deep reflexes are preserved; the knee-jerks may in some cases appear unusually brisk, and, in some cases in which the vastus internus has been hypertrophied, they may be very active. The knee-jerks commonly disappear before the ankle-jerks. The superficial reflexes are preserved and plantars are present and have the normal characters. Sensation is usually perfect to all forms of stimuli, and, though sensory changes have been described in connection with pseudo-hypertrophic paralysis, such alteration must be regarded as exceptional. The control of the sphincters is as a rule normal.

(2) **Juvenile type** (Erb, "Scapulo-humeral").—This type was first described by Erb and it derives its name from the period of life—viz., early youth—at which it most commonly starts. The disease may be present in childhood and manifest itself about the sixth or seventh year of life. This form is both hereditary and familial and affects males and females alike. It is closely related to the facio-scapulo-humeral type—Landouzy-Déjerine—but differs from that in that the face is not affected.

The most prominent feature of this disease is the "winging" of the scapulæ and the difficulty of raising the arms above the head. The winging of the scapulæ is dependent on the weakness of the serratus magnus and trapezius muscles, and the difficulty in raising the arms is dependent on the weakness of the lower portion of the trapezius. Some of the muscles affected are atrophied; others are hypertrophied. The muscles which usually show atrophy are the upper portion of the pectoralis

major and minor, the latissimus dorsi, the lower part of the trapezius, the serratus magnus and the rhomboids. The deltoids, supra- and infra-spinati, usually appear large in comparison to the wasted muscles and may be actually hypertrophied.

As the disease advances, the muscles of the upper arm become affected and show atrophy, those of the forearm remaining normal. Weakness then manifests itself in the muscles of the pelvic girdle and there is wasting of the quadriceps extensors and adductors of the thighs and weakness of the psoas and iliacus group of muscles, so that the child had difficulty in flexing the legs on the abdomen. The muscles of the leg below the knee remain well developed. The degree of atrophy to which a patient may advance, and yet have power to get about, is extraordinary. The face and neck muscles do not become affected. The presence of the deep reflexes depends upon the stage of the disease and the condition of the affected muscles. In the early stages of the disease, the knee-jerks, ankle-jerks and the arm-jerks are present; in the late stages all these disappear.

This type of myopathy is in children the least common of the three types here described. Only a few cases in children under twelve years of age have come under observation, and in none of these was the disease advanced, nor did it make rapid progress.

Trevelyan gives a good account of the disease in a family of eight, in which the father and three children were affected, the first symptoms being noticed in the youngest child when eight years old.

Fig. 469.—Myopathy: Facio-Scapulo-Humeral Type (Landouzy-Déjerine). (With Professor Haushalter's kind permission.)

(3) The facio-scapulo-humeral type (Landouzy-Déjerine).—This type is characterized by a weakness of the muscles of the face and winging of the scapulæ, due to weakness of the muscles of the shoulder girdle. The weakness of the face is especially marked in the orbicularis oris and palpebrarum. It may be present at birth and is sometimes the only sign of the disease for many years. Other features are the weakness and wasting of the muscles of the shoulders and pelvic girdle, and wasting of the muscles of the upper arm and thigh. The disease is both hereditary

and familial, males and females being alike affected, but the familial tendency is by no means so striking as in the pseudo-hypertrophic type.

As seen in infancy, it often escapes notice, and the symptoms which the child presents—viz., the difficulty in sucking the breast or bottle and the fact that it does not close its eyes when asleep—are put down to general weakness. In children of two to three years old, however, the lack of facial expression is very striking. They are unable to raise the eyebrows, unable to close the eyes tightly, unable to blow out the cheeks, or blow a "penny trumpet." The child smiles with its "eyes," but the face remains motionless. The muscles of the eyeball, tongue, palate

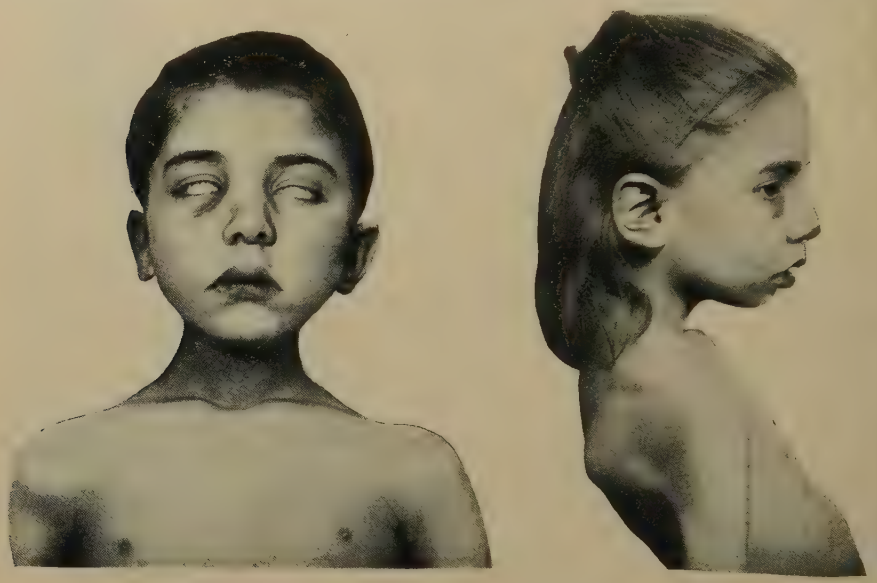

FIG. 470.—MYOPATHY: FACIO-SCAPULO-HUMERAL TYPE (LANDOUZY-DÉJERINE).

The photographs illustrate the marked weakness of the orbicularis palpebrarum and oris muscles. This weakness produces a face devoid of expression. (With Professor Haushalter's kind permission.)

and those of deglutition and phonation are normal and the movements of the head and neck are also good.

A child with such an affection of the face may present no other symptoms of the disease and no further weakness may manifest itself till between twenty and thirty years of age. On the other hand, the weakness of the muscles of the shoulder girdle may show itself at an early age by the winging of the scapulæ. The muscles first affected are the trapezii, the serratus magnus, then the pectorals, latissimus dorsi, biceps, triceps, leaving the deltoid, infra- and supra-spinati and forearm muscles relatively intact. The weakness then manifests itself in the pelvic girdle and is attended by the wasting of the glutei and muscles of the thigh.

Children with this form of disease are often able to get about fairly well. They are able to perform most movements and do not experience

the difficulty of going upstairs, or in getting up from the floor, that is seen in some of the other types of myopathy.

This type of myopathy is one of the most slowly progressive and often seems to remain stationary for years. The case on which Landouzy and Déjerine based their original description died at the age of forty-five, and the disease was known to have existed for over thirty years.

The illustrations taken from Haushalter's excellent paper on the myopathies of childhood illustrate the clinical features well.

(4) **The distal type** (Gowers).—This type, first described by Gowers, is a much less common form. In it, the atrophy commences in the hands and feet, and extends gradually up the forearm and the lower leg. In Gowers' case, the onset was at the twelfth year. The atrophy also affected the sterno-mastoids and there was weakness of the facial muscles.

Pathology.—The muscular changes in the different types are essentially the same. There are large hypertrophied muscles which consist partly of masses of fat lying between layers of fibrous tissue, and there are atrophied muscles, represented perhaps by a thin layer of fibrous tissue, which feel tough and firm. On section some fibres have a diameter of twice or three times the normal but cross striation tends to disappear. Atrophied fibres are reduced to a thin line with a relative or actual increase of darkly staining sarcolemma nuclei. The connective tissue septa are increased.

Diagnosis.—The presence of spinal caries or psoas abscess or poliomyelitis affecting the ilio-psoas muscle must be borne in mind, as children with either of these conditions often give an excellent imitation of the climbing-up-oneself sign said to be so characteristic of the pseudo-hypertrophic dystrophy.

Treatment.—Amino-acid therapy, glycine or glutamic acid, in doses of 10 to 20 gm. a day, may procure a remission or an improvement, or be ineffective, and is not curative. A rapidly progressive myopathy may be made worse when the glycine therapy is stopped.

The amino-acid glycine is a precursor of creatine and as Nevin states in a review of the myopathies there is no rational basis for the use of glycine as a therapeutic agent. Its beneficial action in large doses in a few cases may be that it stimulates metabolism in the healthier or less degenerated parts of the affected muscles.

Vitamin E, in whole-wheat germ, $\frac{1}{2}$ oz. twice daily, has been used, but it is doubtful whether with benefit.

It is essential that the patient be encouraged in the use of his limbs, and not kept in bed. Orthopaedic measures, appliances and tenotomies with enforced rest are rigidly contra-indicated, as by interfering with the active use of the muscles they leave them weaker than before treatment began.

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AMYOPLASIA CONGENITA

Synonyms.—Multiple congenital articular rigidity, arthrogryposis multiplex congenita

Introduction.—This rare condition, of which about fifty instances have been recorded in the literature, is characterised by articular rigidity dependent upon incomplete formation or entire absence of certain muscle groups of the limbs, usually symmetrical. The articular limitation or rigidity chiefly affects the elbows, knees and less often or severely the shoulder, hip, wrist, and ankle joints. The elbows commonly are in fixed extension, the knees in extension or flexion. Spinal rigidity is absent. By radiography, a diminution in size or an absence of certain muscles is demonstrable (Sheldon). The defect involves a group of muscles serving a common function ; for example, the flexors of the elbow when that joint is in rigid extension, or the extensors when it is fixed in flexion.

Fig. 471.—Arthrogryposis Multiplex Congenita.

The knees and hips were flexed right up and the feet were in a position of severe equino-varus. The flexion deformity of the hips and knees has been corrected.

On electrical stimulation the affected muscles do not give a reaction of degeneration, but the response to the faradic or galvanic currents may be reduced or absent. Calcification of the bones is normal, and the articular fibrotic changes appear to be secondary to the muscular defect. Intelligence is normal in these cases, and there is no evidence of sensory or trophic disturbance of the integument. The disease has its onset in intra-uterine life, but is neither hereditary nor familial.

Symptomatology.—The articular rigidity in one or more limbs in extension or flexion is noticed at birth. The infant, however, can fully flex or extend the spine. Various deformities, club-hand and club-foot, may be present.

Pathology.—The muscular defect is probably not of the nature of a true aplasia, but the result of an arrest of development with early degeneration of certain muscle groups. On histological examination of affected muscles, Stopford Price has described striated fibres, fibrous increase and fat replacement, and chains of sarcolemma nuclei, which changes are characteristic of simple muscular atrophy. The muscular

defect is possibly secondary to degenerative changes in the cervical and lumbar enlargements of the cord, but there is, at present, not sufficient evidence to reach a conclusion on this point.

TREATMENT.—Massage and passive movement have in some cases increased the range of movement at the stiffened joints. More often, to obtain a useful degree of articular freedom, orthopaedic measures are required.

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MYOTONIA

This symptom of delayed relaxation of voluntary muscles after natural, mechanical or electrical stimuli is observed almost exclusively in the two disorders, dystrophia myotonica and myotonia congenita. The two conditions can usually be distinguished by differences in age of onset and in the changes occuring in the muscle fibres, but Maas considers them both to be variants of the same disease. The myotonic tendency is transmitted in a dominant manner.

Myotonia is caused by some abnormality at the neuromuscular junction, possibly an excessive production or accumulation of acetylcholine at the motor nerve endings (Russell and Stedman). Acetylcholine injected intra-arterially has no effect on muscle in normal people. In myotonic subjects intramuscularly it has no effect, but intra-arterially acting upon the neuro-muscular junction it promotes muscle contraction. Drugs of use in myasthenia gravis, as prostigmin and potassium chloride which facilitate acetylcholine transmission at the myoneural junction, aggravate the myotonic tendency, whereas quinine hydrochloride has the opposite effect, and reduces myotonia. In myotonia associated with muscle atrophy there is the common upset of the creatine-creatinine balance seen in the muscle dystrophies, while in myotonia without atrophy or congenita there is a raised creatine tolerance and the creatinine content of the urine is a high normal (Nevin).

FIG. 472.—FACIES IN MYOTONIA ATROPHICA.

Dystrophia myotonica; myotonia atrophica. This is the more common form of myotonic inheritance. In a study of ninety-four families of this type, Maas found that 261 individuals had shown signs of the disease, while another 286 members presented suspicious stigmata. When one or other parent is severely affected the number of children per sibship is small, whereas when the parent is only slightly affected average fertility is unaltered.

The characteristic signs in florid cases are myotonia, muscular atrophy, cataract, testicular or ovarian atrophy and loss of weight (Adie and Greenfield). Single stigmata found in other members of the family are mental defect and cataract which may require the slit lamp for its detection. Most cases are dated from the time of obvious muscular weakness, atrophy and cataract, that is, in the third or fourth decade, but Maas states that early signs can be recognized even in infancy and records eight cases diagnosed between the third and fourteenth years.

The feature of myotonia consists of a persistence of muscular contraction after voluntary effort has ceased. Repetition of an action reduces the myotonia. The reaction is commonly noticed in the flexors of the fingers, the patient in grasping is unable to let go quickly. Myotonia of the muscles of the legs and of mastication gives rise to difficulty in walking and in chewing. The wasting of the facial muscles gives rise to an impassive expression—the myopathic facies. In other parts, as in the tongue and the thenar eminence, the prolonged myotonic contraction can be elicited by tapping the muscles with a percussion hammer. The muscles most affected by atrophy are the facial, the masseters, the sterno-mastoids, the muscles of the forearm and hand and the peronei. The tendon reflexes are either diminished or absent. The pupils are dilated and inactive to light but contract slowly on convergence—the myotonic pupil.

Expectation of life is to fifty or seventy years, and the rate at which the patient is incapacitated is very variable. On section, affected muscles show normal, unusually large and atrophied fibres, as in the muscular dystrophies. Quinine hydrochloride in doses up to thirty grains has been palliatively used to relieve the myotonia. Glycine has no effect.

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Myotonia congenita is a rare hereditary disorder affecting both sexes, first described in 1876 by the Danish physician Thomsen, who suffered from it, and known by his name. The myotonia begins early in life and is probably congenital, though it may escape notice until adult life. All the voluntary muscles are liable to be affected, but the muscle-bound reaction on voluntary exertion is usually most obvious in the muscles of the hands, forearms and legs. Repetition of a movement facilitates an easier and quicker performance. There is no wasting of muscles; on the contrary the myotonic muscles hypertrophy, often giving the appearance of exceptional muscularity.

Difficulty in sucking has been observed in an affected infant. On sneezing the eyelids may remain firmly closed for several seconds. In a case of a boy described by Meara, on starting to walk he did so on tiptoe, but after a few steps his gait became more normal.

Quinine hydrochloride has been used as in dystrophia myotonica.

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FAMILY PERIODIC PARALYSIS

In this condition there are periodic attacks of flaccid muscular paralysis, beginning usually in the early morning, lasting a few hours to several days and followed by a rapid return to normal muscular power.

The causation of the periodic paralysis is unknown. It has been found in association with migraine, but there is no evidence of any nervous abnormality. During an attack the potassium of the blood serum is reduced to 10 to 12 mgm. per cent. ; (normal 16 to 20 mgm.). In susceptible subjects this fall and an attack can be effected by the injection of insulin or by large doses of glucose by mouth jointly or separately (Aitkin and Allott). The condition is heredo-familial and has been traced through several generations as in Holtzapple's cases. It is transmitted by either parent, but males are more often affected than females.

In a case personally observed, a woman of thirty-nine years had had three attacks of complete helplessness lasting two to three days, unable to move any limb, but she also had frequent minor losses of power, such as, eyes remaining closed for a few seconds in a cold wind, or the mouth becoming weak for a short period. For some years she had had aching stiff feelings in her thighs and calves and some permanent weakness, without apparent wasting, of the thigh muscles, necessitating her being aided to climb stairs or to mount a bus. All her tendon reflexes were present. She considered provocative factors were cold or damp air, or suddenly coming into a hot room. Potassium therapy had been tried without effect. Her child of three years began at eight months to have phases of weakness lasting about quarter of an hour, in which he was "like an effigy," unable to move a limb, but without any change of colour, and able to cry, or speak as he got older. In the mother's family, she stated her paternal great-grandmother, grandmother, her father, two of his brothers and one sister out of a family of eight children were affected, and also several of the children of the affected members.

The first attack occurs about puberty but may be much earlier. The usual sequence of events is that the patient on waking is unable to move the limbs, the proximal muscles being more affected then the distal. The paralysis spreads rapidly, is usually symmetrical, and in a severe attack may involve the abdominal and respiratory muscles, deglutition and the ocular muscles. The tendon reflexes and electrical excitability of the muscles are temporarily lost, but sensory disturbance is absent, sphincter control unimpaired, and consciousness retained.

TREATMENT.—To counteract the deficiency of potassium in the serum large doses of potassium citrate, 5 grammes repeated, have been given with benefit (Herrington).

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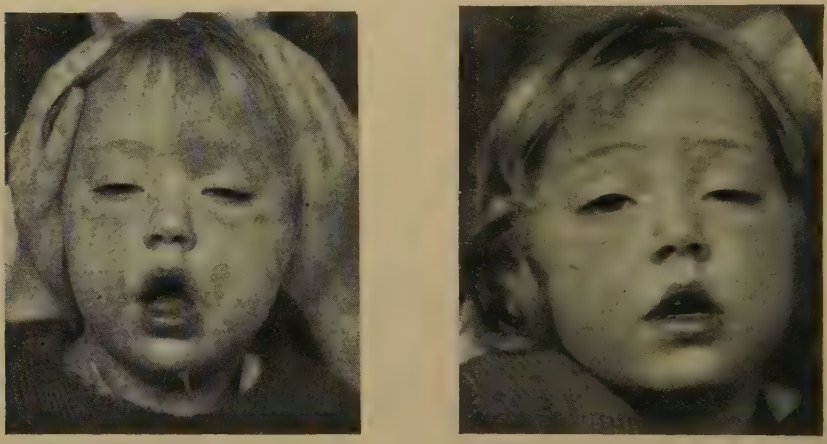
MYASTHENIA GRAVIS

This disease is characterized by a rapid fatiguability of muscles which may first appear in the muscles of the eyes, face, larynx, palate, limbs, neck or trunk. Remissions and relapses are common, and in the later stages permanent muscular weakness in the most chronically affected muscles. It does not appear to be a hereditary disorder, and affects females more often than males.

The age of onset is most often between ten and seventeen years, but instances of infants affected as early as twenty-one and twenty-three months have been recorded. Two cases in girls, with onset at the ages of two and three years, were seen at Great Ormond Street in 1946 (see references). The symptoms in both were fairly similar, firstly, ptosis and



(*a*) (*b*)

FIG. 473.—GIRL OF TWO AND A HALF YEARS WITH MYASTHENIA GRAVIS.
(*a*) Before dose of prostigmin showing ptosis, facial weakness, open mouth and drooling saliva, and (*b*) after prostigmin.

ocular paralyses becoming bilateral, expressionless facies, nasal speech, and at times a tendency to fall on walking, or a weakness in raising an arm. In both a stage was reached of attacks of collapse, cyanosis, difficult breathing due to intercostal paralysis, inability to swallow and drooling of mucus from the open mouth, and excess of moist sounds in the chest. Both responded dramatically to prostigmin, ultimately receiving a maintenance dose of 5 mgm. orally, four or five times a day. Only the ptosis and ophthalmoplegia were resistant to prostigmin therapy, though the mothers stated that after a night's rest the children's eyes temporarily opened normally and with a full range of ocular movements. The thymus was removed in each case by Mr. G. Keynes, and on section appeared normal, weight 17 and 5·5 grammes respectively. The younger girl died several months after operation in a sudden attack of severe collapse.

ÆTIOLOGY.—The fatiguability depends upon a disorder of conduction

at the myoneural junction, which it was thought might be due to a subnormal quantity of acetylcholine liberated at the junction, or to interference with neuromuscular transmission from the presence of an abnormal substance. Wilson and Stoner in myasthenics found that by the exercise of one group of muscles an increase in the fatiguability of an affected group of muscles at a distance could be produced. They further proved that the serum of myasthenic patients not under prostigmin treatment when applied to the isolated nerve-muscle preparation of the frog produced a block in neuromuscular transmission. It appears, therefore, that a substance exists in the blood of patients with myasthenia gravis which opposes neuromuscular transmission, but which can be neutralized or inhibited by the administration of prostigmin.

Pathology.—Changes in the muscles, or muscular atrophy, is rarely seen, and the appearance of the nervous system is usually normal. Lymphorrhages are often found scattered in any of the muscles and in the abdominal organs. In 50 per cent. of the post-mortem examinations hyperplasia, tumour, or persistence of the thymus, though not discernible clinically, has been found (Norris). A relationship between the thymus and the myoneural block has been suggested by the improvement claimed from the operation of thymectomy (Blalock *et al.*). The myasthenic reaction, rapid tiring of a muscle on faradic stimulation which is not produced by the galvanic current, is not a constant feature of this disorder.

Prognosis. Many cases run a prolonged course. In others the disease takes an acute course and the patient dies of respiratory failure, consciousness being fully preserved to the end.

Treatment.—Surgical results in adults from thymectomy are encouraging (Keynes). Muscular exertion is to be avoided and a period of complete rest in bed is advised. Neostigmin benefits the affected muscles temporarily and its effects may be enhanced by giving potassium chloride in large doses 2 to 4 grammes in 2 oz. water, one to three times a day (Laurent). The quantity of Neostigmin varies with each case. In adults it is commonly given two or three times a day shortly before periods of expected activity in doses of 10 to 30 mgm. by mouth or 0·5 to 1·5 mgm. by intramuscular injection. To counteract intestinal colic $\frac{1}{100}$ or $\frac{1}{120}$ grain of atropine sulphate is given by mouth two or three times daily. Proportionally smaller doses will be needed by children, 5 to 15 mgm. orally three to four times a day, or 0·25, 0·75 to 1·0 mgm. subcutaneously six-hourly.

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CHAPTER XXIX

DISEASES OF THE EYES

J. H. DOGGART

General principles of ocular examination

GREAT care is needed in interpreting the clinical history of infantile eye trouble. Thus parents may lack precise memory of its origin, and have sometimes failed to notice which eye appears at fault. Nursemaids, especially if they are untrained, often diagnose non-existent strabismus, thus disquieting every parent within their acquaintance. Nevertheless it is important to gather all the available information, before beginning to examine a baby's eyes.

Unless they are comatose, infants and small children are unlikely to tolerate prolonged dazzling with a bright light, so that examination should be speedy. Apprehensive ones can often be reassured by preliminary chat about the apparatus, and are less likely to fear the ophthalmoscope if they are first allowed to manipulate the switch. Even so, there are many obstacles to a systematic scrutiny of the fundi and media in early childhood. Small children cannot be expected to gaze steadily in a required direction, and inspection of the optic disc is particularly difficult when they keep glancing at the light, so that the macula obtrudes itself. Detailed survey of the fundus may, in fact, be impossible without recourse to general anæsthesia. Unless information about the fundus is urgently needed, a general anæsthetic for this purpose is, of course, contraindicated in the first few months of life, or during illness.

In cases of intense blepharospasm it is essential to ascertain the state of the corneæ, lest there be a perforating wound or ulcer. Before resorting to general anæsthesia, inspection of the eye should be attempted by wrapping a blanket firmly round the child to control his limbs, instructing an assistant to steady the head, and then carefully drawing the eyelids apart by means of retractors. Forcible separation of the eyelids without retractors entails pressure on the globe, with consequent risk of rupture to a cornea already thinned by erosion.

An ocular diagnosis will often be strongly suggested by the history alone. If no such guidance is forthcoming, preliminary search should concentrate on the abnormalities most likely to be encountered at each particular age. In the first few weeks of life, for instance, discharge from both eyes is most frequently the result of mild conjunctivitis ; whereas persistently unilateral discharge at the same stage is more likely to be due to delayed canalization of the naso-lachrymal duct.

In the following account of ocular disorders in childhood, space will be devoted chiefly to those which are commonest in the early years of life. Certain refined methods of examination, *e.g.* subjective testing of refraction, or slit-lamp microscopy, are nearly always difficult or

impossible before the age of five. The fundamental ocular problems are, however, the same in childhood as in later life, so that clinical ophthalmology, in children as in adults, must be founded on a careful record of the history, together with systematic external inspection of the eye and its adnexa, and ophthalmoscopy of its interior.

Congenital abnormalities

Complete absence of an eye is exceedingly rare, but development can be arrested or distorted at any stage, so that the eyeball at birth may consist of incompletely differentiated cells, or may be reduced in size (*microphthalmia*), or may display a cleft (*coloboma*) in one or more of its formed elements.

Dermoid cyst occurs as a round, elastic, non-inflammatory swelling at either end of the eyebrow. Less commonly a cerebral hernia protrudes near the inner end of the eyebrow, but tends to bulge when the baby cries—a feature that differentiates it from dermoid cyst.

Notching of eyelids by colobomata is not common. Distichiasis, *i.e.* duplication of eyelashes, is also rare. Ptosis or drooping of the upper eyelid is usually caused by maldevelopment of the levator palpebræ superioris muscle, and is often associated with similar weakness of the superior rectus, with limited upward movement of the globe as a result. In epicanthus the nasal edge of the ocular conjunctiva is overhung by crescentic folds, which create the illusion of internal strabismus. When the bridge of the nose attains its full development, epicanthus disappears. Angioma, lymphangioma, and plexiform neuroma are occasionally found, but gross congenital deformities of the eyelids seldom arise, unless the globe itself is stunted.

Possible conjunctival growths are lipoma, dermo-epithelioma and angioma, this last-mentioned being as a rule continuous with the palpebral angiomata.

Dermoid cysts may sit astride the corneal limbus, but other corneal opacities in the new-born are usually due to birth trauma.

Coloboma of the iris is one of the commonest congenital ocular deformities. The typical coloboma conforms with the position of the fœtal cleft, and is therefore directed downwards. The pupil is pear-shaped, and the gap in the iris may be partial or complete. A choroidal defect usually accompanies the complete variety. Coloboma of the lens may also be present, and in many instances the cornea is correspondingly pyriform. Aniridia literally means absence of iris, but, in the condition clinically known as aniridia, the iris is in fact represented by a thick peripheral collar which interferes sooner or later with the drainage of aqueous fluid from the angle of the anterior chamber, as proved by the high incidence of glaucoma among the victims of aniridia. This form of glaucoma, however, does not usually become established until adult life, so that the glaucoma that arises in early life is due to an even less permeable drainage angle than occurs in most cases of aniridia.

Heterochromia may affect the whole iris, so that the eyes are of

different colour. Partial heterochromia may be segmental or sectorial in its distribution. Aplasia of the pigment layer is found in albinos. Congenital inequality of pupils (anisocoria) is not very uncommon. Marked eccentricity of pupils can occur in otherwise normal eyes. Multiplicity of pupils is known as polycoria. At least 25 per cent. of infants show persistent pupillary membrane, due to incomplete atrophy of the anterior vascular sheath of the lens, which covers the pupil during fœtal life. In most cases these remnants do not appreciably interfere with vision, because they consist merely of a few tenuous strands arising from the collarette of the iris. Such strands may float free in the anterior chamber, or may extend across the pupil, to gain attachment to the opposite side of the iris. They are often associated with pigmented stars on the anterior lens capsule. Occasionally dense fibres persist, mechanically obstructing vision in one or both eyes, and these are liable to be misinterpreted as posterior synechiæ due to old iridocyclitis.

Rarely the whole lens is absent. It may be notched by a coloboma, or displaced (ectopia lentis) by irregular formation of its suspensory ligament. Of the various forms of opacity (cataract) present at birth, many are localized, stationary, and not large or dense enough to interfere seriously with vision. Complete opacity of the lens at birth seldom occurs in the absence of severe developmental or inflammatory lesions affecting other parts of the eye. Maternal rubella is one possible cause of congenital cataract.

Dense vitreous opacities at birth are attributable as a rule to birth trauma or to intra-uterine uveitis. Some cases of persistent hyaloid artery show dense offshoots of tissue extending laterally through the vitreous, but in the majority of cases the hyaloid vessel is represented at birth merely by a small tag of tissue attached to the posterior lens capsule, or to the optic disc—the intervening vitreous portion having undergone atrophy.

Coloboma of the choroid is displayed as a white area continuous with the optic disc. Its typical direction is downwards, like that of an iris coloboma, with which it is usually associated. Colobomata of the optic disc are frequently continuous with those of the choroid, but can occur as an isolated feature in the form of a small inferior crescent (Fuchs' coloboma). Deep holes, single or multiple, are sometimes found on the optic disc. Wisps of connective tissue obscuring some or all of the vessels on the disc, or bridging over the physiological cup, are harmless, though they are often mistaken for exudate or œdema. Peculiar arrangements of the retinal vessels occur in great variety without impairing function.

Many babies are born with traumatic retinal hæmorrhages, which usually absorb without permanent damage. Small patches of heaped-up pigment cells (innocent melanomata) may come to light in routine examination of the fundus. Intra-uterine toxoplasmosis can produce large central and peripheral areas of choroido-retinal atrophy and irregular deposits of pigment. Opaque nerve fibres are not, strictly speaking, congenital, because the process of myelination involving some of the optic nerve fibres anterior to the scleral ring is not completed until a few days after birth. Such fibres are displayed as a distinct white striation on the

surface of the retina, in most cases adjacent to and continuous with the optic disc, but are occasionally found in the periphery of the fundus. Partial aplasia of the retina is a feature of albinism.

Ocular complications and sequels of other diseases

Conjunctivitis is almost invariably present during measles, and, if neglected, may be the forerunner of corneal ulceration and blepharitis. Small-pox, scarlet fever, influenza and many other acute infectious illnesses may also give rise to inflammation of the conjunctiva and cornea. Whooping-cough commonly produces hæmorrhage in the conjunctiva, and occasionally in the retina. Paralysis of accommodation may appear during convalescence from diphtheria.

Septic teeth and tonsils probably predispose to keratitis. Lamellar cataract is often accompanied by hypoplasia of dental enamel. Diabetes does not lead to fundus lesions in children, but is sometimes the cause of a characteristic, rapidly developing type of cataract. Exophthalmia results from Graves' disease.

Retinal hæmorrhages occur in all forms of severe anæmia. In severe blood diseases, *e.g.* the leukæmias, the hæmorrhages often consist of closely aggregated white cells haloed by red corpuscles. Papillœdema from raised intracranial pressure is often associated with hæmorrhages on or near the optic disc.

Tuberculosis is not only an important contributory cause of phlyctenular disease, but is also responsible for certain forms of chronic conjunctivitis, uveitis and lachrymal disease. Gonococci are the commonest organisms found in *severe* cases of conjunctivitis in the new-born. Syphilis may cause intra-uterine iridocyclitis, and is also responsible for interstitial keratitis.

Diseases of orbit

Enveloped in fat, and retained in position chiefly by the optic nerve and the extraocular muscles together with their check ligaments, the eye rests in the orbital cavity, where it is traversed by vessels and nerves. Thin layers of bone separate the orbit from the cranial cavity, the nose and the accessory sinuses.

The new-born eye is already three-quarters grown, and is thus readily displaced from the relatively small infantile orbit. Moreover the corneo-scleral coat of the eye is more easily distended in childhood than among adults. Undue prominence of the eye may be due to :

(1) Increase in the size of the eye itself, as in high myopia or in juvenile glaucoma.

(2) Relaxation of supporting structures, as in total ophthalmoplegia—although prominence of the globe from this cause is masked by ptosis.

(3) Decreased size of the orbit, *e.g.* in hydrocephalus, oxycephaly and hereditary cleido-cranial dysostosis.

(4) Forward thrust of the eye by orbital swelling, whether fluid or solid in nature.

Fluid swelling may consist of inflammatory effusion, as in orbital cellulitis, or cystic tumour, *e.g.* cavernous lymphangioma, or extravasated blood from injury or hæmophilia. Examples of solid swelling are provided by various tumours, *e.g.* sarcoma, growths of the optic nerve, Hutchison's tumour, chloroma and the Schüller-Christian xanthoma. Chloroma is bilateral, and is associated with the presence of myelocytes in the blood. Graves' disease is a rare but important cause of proptosis in childhood.

Orbital cellulitis may arise from injury, especially when a foreign body is retained, or by direct extension from infected air-cells, or by metastasis in systemic illness. Swelling arises in the lids and conjunctivæ, the eyeball is pushed forward, and its movements are limited in one or more directions. Pain and raised temperature are other features. According to Negus, external incision is seldom advisable, and the origin of the trouble is usually in the frontal sinus or ethmoidal air-cells, necessitating antral lavage and ephedrine sprays. If incision is considered necessary, the best situation is at the inner end of the lower orbital margin. Premature or misplaced incisions probably increase the liability to thrombosis of the cavernous sinus, a serious complication.

Backward displacement of the eye is an occasional result of comminuted or unreduced fractures involving the orbit. Cellulitis followed by cicatricial retraction is another possible cause. Horner's syndrome in lesions of the cervical sympathetic leads to miosis, ptosis and enophthalmia on the affected side, but the last-mentioned feature is in reality slight. Ptosis increases its apparent degree.

The *diagnosis* of orbital disease presents many difficulties, and, in cases that remain obscure after careful history-taking and clinical examination, X-ray photographs and blood investigation are often illuminating. Surgical exploration of the orbit to establish a diagnosis is less often needed in children than in grown-up people.

Refraction

The fine adjustment of refractive results by subjective testing is seldom possible before the age of five years, and may be difficult in children older still. Moreover the immediate reason for refraction in many children is a squint, whose presence demands accurate correction of astigmatism, as well as the over-correction of hypermetropia in the accommodative variety of strabismus. For these and other reasons no one should prescribe glasses for children before acquiring considerable experience among adults.

Mydriasis and cycloplegia are best obtained by the use of 1 per cent. atropine ointment in both eyes twice daily for four days. In the absence of squint, it is unnecessary to correct small amounts of hypermetropia, because children are normally hypermetropic in the first few years of life. Nor is it desirable to banish children from books on account of moderate myopia, which is neither caused nor augmented by reading. Myopia arising before completion of bodily growth undergoes some increase in over 90 per cent. of people, whether they read all day, or gaze vacantly into space. Charlatans claim that their expensive exercises will cure myopia. No cure has in fact been discovered.

Squint

In the early months of life, before binocular reflexes are elaborated, transient squint need not signify anything untoward. Pronounced and permanent squint in early infancy usually indicates abnormal insertions or imperfect development of one or more of the extraocular muscles. Variable and fleeting squint may occur in meningitis. Raised intracranial pressure and trauma are other possible causes, but the great majority of children's squints are concomitant, not paralytic, and the usual age of onset is two to six years.

The most important factors in the ætiology of concomitant squint are refractive errors, general weakness, heredity and nervous instability. Obviously there is a large overlap between the last two factors. In many cases the decisive influence of refractive error is proved by immediate neutralization of the squint when appropriate glasses are supplied. Thus measurement of the squint with and without glasses is desirable, though it must be remembered that the angle varies considerably in certain cases, quite apart from the variation due to glasses.

In properly selected cases orthoptic treatment is of great value. When the angle is large, say 30° or over, operation will probably be needed, but exercises are useful not only as a preliminary measure, but also post-operatively, to consolidate a successful result, or to abolish any small residual angle of deviation. Unilateral squints of long standing often show serious diminution of vision (amblyopia) in the misdirected eye. Orthoptic training is, of course, inapplicable until the amblyopic eye is compelled to see. Covering up the sound eye for *part* of each day will *not* achieve this end. *Complete* occlusion for weeks or months is essential, until the exposed eye sees almost as well as its fellow. A black disc worn in front of the spectacles is ineffective, because a child soon learns to look round the corner. Gauze pads, controlled by strapping, should be employed, after lubrication of the lid margins with vaseline. Occlusion often effects another desirable change—the abolition of that false projection (abnormal retinal correspondence) which many squinters adopt as a compensatory mechanism.

Poor progress after provision of suitable glasses, combined with orthoptic treatment, is often explained by unhappy home circumstances, leading to fear, jealousy and other disturbed emotions. Unless some radical change can be brought about, it is useless to continue exercises, because, in order to benefit thereby, the victim of strabismus must have equanimity, as well as adequate will-power and intelligence.

Injuries

For medico-legal reasons it is important to record the visual acuity of an injured eye as soon as possible, although the immediate vision is not a measure of the severity of the lesion. Thus an iris hæmorrhage may at first reduce vision to less than 6/60, with full restoration a day or two later; whereas an early detachment of retina, or even the presence of an

intraocular foreign body, is quite compatible with 6/6 vision for a time. Contusion from blunt instruments seldom needs more treatment than rest and atropine, but a guarded prognosis in the early stages is justified by the great variety of possible damage that may subsequently be revealed. In perforating wounds careful search must be made for prolapse of uveal tissue or other contents of the globe. Wounds of the lens call for special vigilance. In most cases of persistent irritability associated with entanglement of uveal tissue in the wound, removal of the eye becomes imperative, to obviate the disastrous complication of sympathetic ophthalmia in its fellow.

Nystagmus

A few abortive jerks on extreme version of the eyes to either side is often misinterpreted as nystagmus. True nystagmus implies rhythmical oscillation of one or both eyeballs, and may be hereditary. The labyrinthine variety, which occurs in certain diseases of the central nervous system, as well as in lesions of the labyrinth itself, is of medium speed, and approximately twice as rapid in one direction as in the other. Ocular nystagmus, on the other hand, may be slow or fast, but is always pendular, *i.e.* the to and fro components are of equal pace.

Ocular nystagmus is usually the result of interference with fixation. This faculty can be acquired only in the first few months of life, and if it is obstructed, *e.g.* by dense bilateral cataract at that period, subsequent operation, however successful in other respects, does not abolish nystagmus. In some cases of squint or fundus disease, nystagmus is latent, *i.e.* only becomes manifest when one eye is covered. Nystagmus in albinos is occasioned by retinal aplasia.

Eyelids

Inflammation of the lid margins (blepharitis) is provoked by local infection or by some form of irritation, which may be allergic. Refractive errors are *not* to blame. The most severe cases occur as a sequel to neglected conjunctivitis in measles. If crusts derived from conjunctival discharge are left adherent to the lashes for days at a time, the resulting inflammatory process tends sooner or later to involve the hair follicles. Ill-advised plastering with ointment, and repeated application of silver nitrate, can only prolong the trouble.

The *treatment* of blepharitis is simple. All crusts must be removed from the eyelashes by sponging with clean wool moistened by warm water, or, in firmly encrusted cases, by hydrogen peroxide. In mild forms cold cream should be gently massaged into the eyelids at bedtime. Pigmentium tinctorium, applied with a brush thrice daily, is an excellent remedy when the blepharitis is more severe. The resulting violet coloration of the skin fades within a few days of the final application. Encouraging results have also been obtained with penicillin cream. When blepharitis is associated with a seborrhœic scalp, the latter condition should be regulated by a spirit lotion.

Meibomian cysts present no special features in children. Styes, which

are very common, have been wrongly attributed to refractive errors and to various disturbances of general health, but in practice they commonly arise in emmetropic children glowing with health. When once a stye has begun, it will run its course for a few days, whatever treatment is adopted. Therefore no benefit accrues from incisions and caustic applications. Frequent fomentations serve only to prepare the skin for a further crop of styes. A stye should be left alone until it comes to a head. When it bursts, the contents should be gently sponged away with a mild antiseptic lotion, *e.g.* mercury oxycyanide, 1 in 12,000. If styes persistently recur in the absence of any remediable disturbance of general health, a staphylococcus vaccine affords a chance, though not a guarantee, of cure.

In all disorders of the eyelids the golden rules should be to interfere as little as possible with these most sensitive portions of the skin, and to eschew sticky ointment.

Lachrymal disorders

The lachrymal gland, which lies near the outer end of the upper orbital margin, is occasionally invaded by tuberculosis, which may in other cases attack the lachrymal sac and the naso-lachrymal duct, with or without intranasal lupus. The commonest cause of lachrymal mucocele in infants is, however, delayed canalization of the naso-lachrymal duct, as revealed by the onset of epiphora and mucous discharge from one eye a few days after birth. In the great majority of cases canalization is spontaneously completed within a year, so that probing is rarely necessary. Pending canalization, treatment consists of irrigation several times daily, preceded on each occasion by gentle expression of accumulated mucus from the sac.

Conjunctiva

Conjunctivitis of the new-born is rarely established before the third day of life, and is in most cases due to staphylococci or other non-virulent organisms. Gonococcal infection is far less common than it was a generation ago, but still demands special precautions, as a major cause of blindness. The instillation of one drop of 5·0 per cent. mild silver proteinate into each eye at birth, preceded by careful wiping of the skin of the eyelids, may entail slight conjunctival congestion for a few days, but this is a trivial disadvantage, contrasted with the benefit of so effective a measure of prophylaxis, which is therefore recommended as a routine whenever the birth-passages are suspect. On the other hand, mild silver proteinate and similar preparations are contraindicated in *established* cases of acute conjunctivitis, gonococcal or otherwise. The use of silver nitrate as treatment is dangerous. Even as a prophylactic, this substance is inferior to mild silver proteinate.

Acute conjunctivitis of the new-born is heralded by profuse discharge about the third day. Local treatment consists of irrigation with tepid normal saline to clear away this discharge, which, if undisturbed, gums the lids together, so converting the conjunctiva into a warm, closed sac suitable for the multiplication of organisms to menace the cornea. The

interval between each irrigation may be anything from a few minutes to several hours, according to the stage and severity of the inflammatory process. Lubrication of the lid margins with liquid paraffin will diminish their tendency to stick together during sleep, but the main desideratum is to flush away the discharge before it has accumulated in large amount.

Mild cases clear up within a few days, but gonococcal infection requires more prolonged attention. In the early stages of this disease (often called ophthalmia neonatorum), the discharge is sero-sanguineous, and is accompanied by intense swelling of eyelids, which must be carefully manipulated to avoid corneal abrasion. It is impossible for one person to irrigate gently and thoroughly without an assistant to hold the infant steady. The proper care of severe conjunctivitis in a baby consumes so much time, that such cases should, if possible, be sent with their mothers to specially equipped hospitals. Penicillin is a valuable remedy in the local treatment of these cases and has largely superseded sulphonamide therapy.

Epidemic conjunctivitis in schools is usually due to the Koch-Weeks bacillus, and is characterized by profuse muco-purulent secretion, together with intense conjunctival infection. Spontaneous hæmorrhages often arise in the conjunctiva, but corneal complications are rare. This variety of conjunctivitis, and that which occurs in measles, both respond well to simple treatment. Mercury oxycyanide, 1 in 12,000, or, if this is unobtainable, normal saline solution, is appropriate for irrigation several times a day. Lid margins should be lubricated at night, and crusts removed by sponging with moist cotton-wool. Drastic remedies, *e.g.* repeated application of silver nitrate, increase discomfort, prolong the attack, and may result in blepharitis. Neglect may be responsible for similar consequences.

Tuberculous conjunctivitis, spring catarrh, and trachoma, are less common in Great Britain than the above-mentioned disorders, but should always be borne in mind as possible diagnoses in difficult cases. The adequate treatment of trachoma in children can only be achieved in special institutions.

Phlyctenular disease

This condition was widely believed to be tuberculous in the nineteenth century, but repeated failure to demonstrate the tubercle bacillus in a phlyctenule discredited that theory. Sorsby and others have, however, resuscitated the doctrine in a different form. They maintain that, although phlyctenules may be due to a variety of immediate or exciting causes, *e.g.* the staphylococcus or minor trauma, yet such precipitating factors are fruitful only when they alight on sensitised soil, and that sensitisation is effected by the tubercle bacillus in at least two-thirds of cases of phlyctenular disease.

Certainly the improvement in working-class standards of living, coupled with closer supervision of school children during the last three decades, has been marked by a fall in the incidence of phlyctenular disease. True phlyctenules are hardly ever seen in a healthy home, and the typical phlyctenular child shows infestation of the hair with nits, tonsillar infection, and evidence of inadequate diet. Thus attention to general health is

most important in the treatment of phlyctenular disease. Locally the use of dark glasses is supplemented by irrigation with normal saline or some other weak lotion. Implication of the cornea (fig. 474) calls for

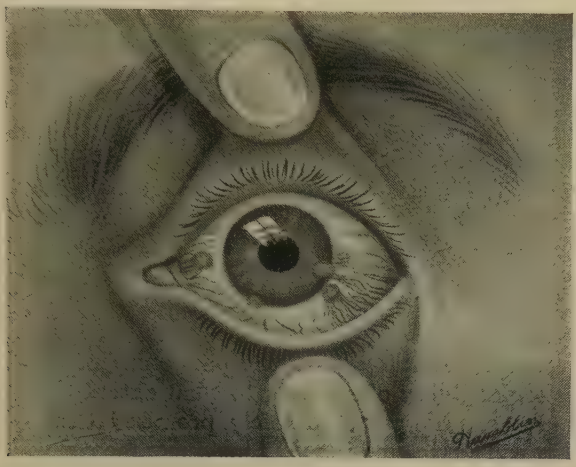

Fig. 474.—Phlyctenular Kerato-Conjunctivitis.

1·0 per cent. atropine. Most cases respond very well to simple remedies, so long as cleanliness, fresh air and adequate diet are obtainable. When these are lacking, the disease may recur time after time, until sight is permanently obscured by dense, vascularized corneal scars.

The cornea

This structure is vulnerable to most of the organisms that afflict the conjunctiva, *e.g.* gonococci, streptococci, so that ulcerative keratitis may emerge as a complication of conjunctivitis from such agents. Abrasion of the cornea readily becomes an ulcer if resistance is lowered. Measles and several other epidemic illnesses can also cause ulceration, with or without premonitory conjunctivitis.

Resistance to infection on the part of the cornea is largely determined by the level of general nutrition, and the most unfavourable prognosis applies to children suffering from vitamin A defect. In healthy children the cornea reacts violently to a noxious influence, so that pain, photophobia and redness of the affected eye are prominent features of corneal ulceration. Such reaction is conspicuously absent under stress of famine, when both corneæ may melt painlessly away. Other predisposing or aggravating factors are dirt, dust and glare.

It follows that hygienic and dietetic measures are an essential part of treatment in corneal ulceration. A course of general ultra-violet light may also help, but is less effective than cleanliness, ventilation and proper food. Local remedies are dark glasses or loose shades, irrigation with weak lotion, *e.g.* 1 in 15,000 mercury perchloride, and 1·0 per cent.

atropine drops. Carbolization is rarely needed in children. Sulphonamides and penicillin are valuable in certain cases.

Interstitial keratitis in congenital syphilis always affects both eyes, though an interval of several weeks usually elapses before initial signs emerge in the second eye. Some cases arise insidiously with slight painless haze of the cornea. Others display sudden redness and photophobia. The characteristic vascularization in this disease involves the deeper layers of corneal substance after an interval. Diagnosis is often confirmed by the family history, and by the stigmata of congenital syphilis in other parts of the body. Fundus lesions consist of multiple foci of peripheral choroiditis. These are not easy to see until the acute stage of the disease has settled, but they serve to remind us that interstitial keratitis is incompletely named, because the inflammatory process involves the whole uveal tract, *viz.* iris, ciliary body and choroid, as well as the cornea.

The prognosis concerning ultimate vision in a case of interstitial keratitis is rendered difficult (*a*) by the possibility of recurrent attacks, and (*b*) by the impossibility of knowing to what extent the corneal opacity will resolve. It can, however, be safely promised that some degree of corneal clearing will ensue, and in many instances recovery of sight exceeds expectation. Dark glasses and atropine are indicated for local treatment, though full mydriasis is seldom achieved, owing to the presence of plastic iritis. Whether general anti-syphilitic remedies can shorten or alleviate an attack of interstitial keratitis is a controversial question, not yet settled. On general grounds, however, a course of anti-syphilitic treatment should be started forthwith.

Lens

Strictly speaking, every dot of opacity in the lens constitutes a cataract, and the morphological range of variety is infinite, but, for practical purposes, they can be divided into three main types :

(1) Small, stationary opacities, not interfering appreciably with sight.

(2) Dense cataracts associated with grave developmental defects or serious inflammatory disorder involving other parts of the globe.

(3) Lamellar cataract.

Treatment is not usually indicated, except in the last-mentioned type.

The lens continues to grow throughout life by forming successive layers of epithelium within its capsule. Opacification of a group of layers may be one of many bodily responses to some nutritional crisis, the resolution of which allows the formation of transparent fibres to be resumed. Thus lamellar cataract implies the presence of an opaque zone sandwiched between transparent fibres. Rarely two separate zones of opacity have been observed, corresponding with two separate periods of illness or malnutrition. The parallelism between lenticular development and general metabolism is shown by the frequent association of lamellar cataract with calcium deficiency.

If the cataract is dense enough to interfere seriously with vision,

needling is performed, so as to expose the lens fibres to the solvent action of the aqueous fluid. This operation may have to be repeated two or three times in each eye, but good sight is usually obtained with the aid of strong convex glasses. In a certain proportion of cases both retinae become detached many years after needling for lamellar cataract, but the mechanism of this dreaded sequel is not clearly understood.

Uveal tract

The vascular, pigmented middle coat of the eye comprises, from before backward, the iris, ciliary body and choroid, known collectively as the uveal tract. All these structures are implicated in sympathetic ophthalmia

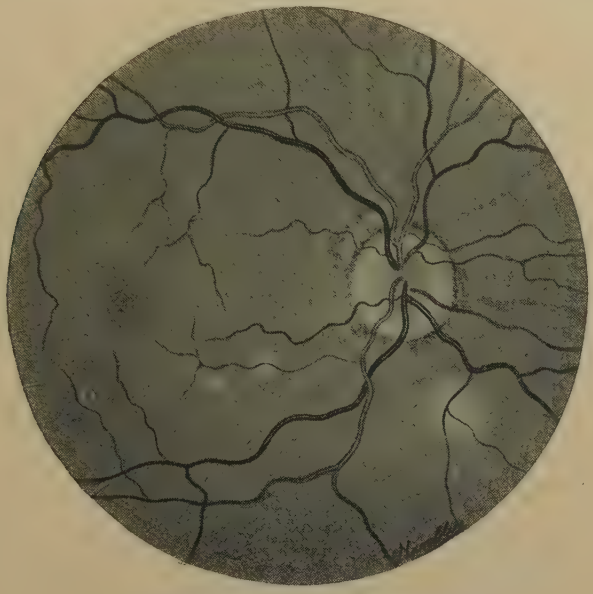

Fig. 475.—Miliary Tubercles of Choroid.

and interstitial keratitis, and the same triple involvement may be due to other conditions. In the absence of trauma or corneal ulceration, syphilis is nearly always the cause of infantile uveitis, and may originate before birth. Large patches of central pigmentary degeneration are in some text-books designated as macular coloboma, but this term, implying as it does, anomaly of development, is misleading. The lesion is clearly caused by intra-uterine choroiditis. In fully established retrolental fibroplasia, of which the victims are as a rule premature infants, atrophy of the iris occurs in association with partial lenticular opacity and dense strands of connective tissue in the vitreous. At an earlier and reversible stage of this disease ophthalmoscopy reveals tortuosity, dilatation and hæmorrhages of the peripheral vessels of the retina. Unless the disease can be arrested, retinal detachment supervenes, and then the associated exudate

becomes organized into connective tissue occupying the vitreous chamber (Reese and Blodi, 1951).

Tuberculosis attacks the choroid (1) as one aspect of acute miliary tuberculosis, forming multiple cloudy, yellowish deposits, smaller than the optic disc, and scattered about the fundus (see fig. 475); (2) in the form of a massive tuberculoma fungating into the vitreous.

Most choroidal lesions are visible to ophthalmoscopy, because the overlying retina is normally thin and transparent. All forms of choroiditis involve the retina, the posterior layers of which depend for their nutrition upon the vessels of the choroid. Consequently no sharp demarcation can be agreed between choroiditis and retinitis, so that the expression choroido-retinitis, though cumbersome, is often the most accurately descriptive.

Retina and optic nerve

Trauma and blood diseases have already been mentioned as possible causes of retinal hæmorrhages in early life. Increased intracranial pressure also tends to cause them. Renal retinitis, a bilateral condition arising in certain severe cases of chronic nephritis, induces failure of vision, associated with large flame-shaped hæmorrhages, snow-bank exudates, retinal detachment, and star figure at the macula.

In *amaurotic family idiocy* the macular lesion consists of a cherry-red spot in both eyes, associated with optic atrophy and deterioration of mind and body, with a fatal outcome. Most victims are Jewish, and the onset is in the first three years. *Batten's disease* is a further example of progressive cerebro-macular degeneration displaying familial incidence, but without any predilection for Jews. It tends to begin later, *i.e.* from the age of three to seven years, and the fundus picture is less consistent than that of amaurotic family idiocy. The typical macula of Batten's disease is faintly stippled, but sometimes gross pigmentary accumulations are seen. Moreover the changes are not always confined to the maculæ, so that peripheral degeneration may be detected. Severity of prognosis is inversely proportionate to the age of onset, so that, when macular signs are first manifested after puberty, they may be unaccompanied by cerebral disease.

Retinitis pigmentosa is an important cause of familial night-blindness, though symptoms may be slight or absent until adult life. The eye changes consist of tapering, bone-corpuscle-shaped figures of pigment gradually spreading from the mid-periphery to involve the whole fundus. Shrinkage of retinal arteries, and waxy-looking atrophy of the optic disc are additional features, and advanced cases are complicated by cataract. Occasionally the peripheral fundus changes of retinitis pigmentosa are simulated by Batten's disease or by syphilitic choroido-retinitis.

Glioma of the retina is bilateral in about one-third of the cases, though an interval of months or years may elapse before its appearance in the second eye. It is a malignant retinal neoplasm (see fig. 476), affecting babies or young children, and threatening life by extension into the brain viâ the optic nerve. Within the eyeball it tends to grow forward through

the vitreous, pushing the lens in front, so as to produce secondary glaucoma in neglected cases. Growth may be so rapid that small detached fragments may sink to the bottom of the anterior chamber, like a hypopyon. A phosphorescent effect may be produced by the vitreous masses, so that parents may notice the affected eye "looking like a cat's eye in the dark." Tissue sprouting in the vitreous may be so marked a feature in metastatic panophthalmitis, or in conglomerate tubercle of the choroid, as to induce suspicion of glioma. The affected eye is in such cases, however, completely disorganized, so that its removal is justified, when the fatal consequences of neglected glioma are taken into consideration.

Optic atrophy is a necessary result of any extensive fundus disease,

FIG. 476.—GLIOMA OF RETINA.

and a sequel to papillœdema, but in many instances it is detected during routine examination without being adequately explained by the history or by clinical signs elsewhere. Doubtless birth trauma accounts for many such cases. Atrophy may, of course, be partial or complete. If it is bilateral as well as complete, attention will be drawn to the purposeless roving of the affected infant's eyes before he is many months old.

Papillœdema can develop rapidly in children. Cases occur in which, though the presence of intracranial neoplasm is rendered certain by other evidence, yet normal optic discs are found. Repeated scrutiny of such cases, however, at frequent intervals, have afforded proof that several dioptres of swelling can arise within a day or two. Blurring of the disc edges, although it invariably affects at least some part of the circumference in papillœdema, does not *of itself* indicate swelling. In many cases of compound hypermetropic astigmation, and even without any refractive

error, the margins of the discs may be blurred without any disease being present. Genuine swelling is betrayed chiefly by the fact that the lenses required in the ophthalmoscopic sight-hole to display the summit of the disc in the utmost clarity of detail are *relatively* convex, compared with those that suffice for the fundus immediately adjacent to the disc. Slight elevation of the disc from heaping-up of nerve-fibres is a physiological sign in small hypermetropic eyes, so that no swelling of less than a dioptre is of pathological significance *as such*. Subsidiary signs in early cases are alteration in the light reflex of vessels crossing the disc margins, and obliteration, total or partial, of the physiological cup. Turgidity of retinal veins is another fairly early sign, followed by hæmorrhages on or near the optic discs, and sometimes exudates, especially when the swelling rapidly increases. There may also be folds radiating from the fovea centralis to the disc, like the spokes of a fan.

Measurement of blind-spots on the Bjerrum screen, and charting the peripheral fields of vision, occasionally provide useful information in older children, unless the causative lesion has impaired their capacity for concentrated attention.

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CHAPTER XXX

DISEASES OF BONES AND JOINTS

A. V. NEALE

DISEASES OF BONES

General introduction. In considering disease of, or affecting, bone, certain facts must be kept in mind. The physiological development and maintenance of bone is clearly understood. The regularity of epiphyseal and diaphyseal progression from the chronological exactitude of ossification centres allows a strict comparison when the abnormal is presented. The activities at the epiphyseal line and the moulding in size, shape and length of the metaphyses and diaphyses in long bones follows regular laws as body growth proceeds. The trabecular arrangements are developed to meet particular stresses and strains in various parts of the skeletal system. Bone is potentially a very labile tissue, possessed of considerable vascularity and the site of some remarkable chemical activities.

Cellular activity, in developing bone, centres round osteoclastic or osteoblastic functions within special media wherein acid-base reaction, ionization of salts, concentration and deposition of salts and phosphatase enzyme are all concerned with the final processes of ossification. Provided adequate vitamin D, and carbonate and phosphate of calcium, are present and available in the body, bone formation keeps pace with general development. In mature bone the ratio of $CO_3 : PO_4 :$ Ca is 1 : 6 : 10, but the relationship differs somewhat during the period of growth, and in callus. The extreme hardness and nature of the solid matter in bones is important in regard to mechanical stability, and it is of interest that the above ratio of carbonate and phosphate favours the chemical integrity and hardness.

Physiological economy dominates the optimal concentration of inorganic salts and matrix within the osseous system, so that it is possible readily to determine radiologically the normal density and trabecular formation. However, osteogenesis may be subject to modifying influences of wide and varied character, *e.g.* genetic, hormonal and metabolic. It is in the study of such aberrations that much of present-day knowledge has been obtained. Clinical description of bone disease and deformity can be found in ancient writings, but it is only within relatively recent years that a classified grouping has been possible through careful clinical, biological, histological and radiological examination. The labile character of the mineral storage in bone is indicated under conditions whereby withdrawal occurs as in hyper-parathyroidism, or in the several processes leading to osteoporosis, local or general. Sometimes the opposite process, osteopetrosis or osteosclerosis occurs and may be associated with change in fragility. The disruptions in the active areas of bone development as revealed in rickets and scurvy and their remarkable

reversal on correcting the vitamin deficiency indicates the powerful influences which these vitamins exert on the regular tissue changes normally operating at the lines of bone growth. Certain degrees of inadequate osteoblastic function are related to imperfect osteogenesis ; or excess osteoclast activity may be responsible in certain cystic forms of bone disease.

Some remarkable examples of distortion in the regular progression of epiphyseal-metaphyseal development are known. Medical literature is well sprinkled with examples, but unfortunately such an array of different descriptive terms has evolved that simplification is desirable ; here the name *chondrodysplasia* will be used. Herein are found numerous irregularities and often bizarre deformities at the ends of the long bones and certain types are recognizable on clinical inspection of the patient. *Achondroplasia* may represent a state of early failure in the zone of proliferation at the epiphyseal cartilage.

Disorder within the skeletal system is observed in several diseases of widely distributed character in the body and this is exhaustively considered by Fairbank (1951). In this respect they cannot be considered as diseases of bone, but examination of the osseous system by radiology may yield important diagnostic evidence. *Skeletal lipoidosis, e.g. Hand-Schüller-Christian disease* ; *cholesterosis* ; *Gaucher's disease* and *gargoylism*, will be considered. *Sarcoidosis* reveals osseous lesions. The metabolic unrest in chronic nephritis leads to characteristic bone changes. Hæmatopoietic disease such as chronic hæmolytic anæmia and leukæmia may yield informative radiological effects in the long bones or in the skull (Teall, 1939). Some evidence of the intensity or the progress of bone manifestations in the juvenile type of rheumatoid arthritis can be followed. Cretinism and juvenile myxœdema have important reflections in the skeleton. Under the term *fibrous dysplasia*, an associated syndrome of precocious puberty, with cystic bone disease and brown skin pigmentation, is now known ; this has given rise to some profound thought on the possible relationships of bone pathology to the hypothalamic-pituitary central mechanisms. Congenital syphilis, tuberculosis and pyogenic infection may be principally concerned with epiphyseal and diaphyseal disease. *Osteochondritis juvenilis* forms an interesting and very important group of epiphyseal affections, the ætiology of which has led to variable opinion on local and general causes. The possible linking together of dysplastic abnormalities of the skeleton and other tissues is noted by Parkes Weber, who gives instances of the combination of osteopoikilosis with scleroderma ; osteopetrosis with congenital dysplasia of the skin ; chondrodystrophia calcificans congenita with atrophodermia ; chondrodysplasia and congenital morbus cordis ; and chondro-ectodermal dysplasia (Weller, 1951).

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Achondroplasia

Synonyms.—Chondrodystrophia fœtalis, micromelia.

Definition.—A disease usually of fœtal life, characterized by shortness of the long bones, trident hands, and large head. It depends on defective evolution of chondral ossification, especially at the extremities of the long bones.

Although earlier observers, such as Muller (1860) and Urtel (1873) recognized that the disease was not ordinary rickets, Parrot (1878), first definitely separated it from rickets and from cretinism, and called it "achondroplasia." The striking characteristics of achondroplasia can be recognized in the representations of the Egyptian gods Bes and Phtah, and of various court dwarfs. Achondroplasia has existed for at least 5,000 years in Egypt (Ruffer). Latent and incomplete forms of achondroplasia have been called chondrohypoplasia (Ravenna).

Ætiology.—Heredity.—Delivery in achondroplasic women usually necessitates Cæsarean section, and so interferes with the propagation of an achondroplasic race. The disease may be handed down through the male line, and its occurrence in males in three generations has been recorded (Peloquin, Porter). Hunter found a father, son and son's daughter affected. A pedigree given by Robin and Weill showed achondroplasia in the first and fourth generations, and partial achondroplasia in the second and third generations on the male side. The disease may also be familial, but of twins one may be achondroplasic and the other normal. Certain species of animals, such as dachshunds and Ancon sheep, have been regarded as examples of achondroplasia fixed by inheritance, but the "bulldog" calves also described as achondroplasic have been shown by Seligmann to be cretins. It is often stated that the disease is more frequent in females than in males, and of Kassowitz's collection of twenty-nine cases four only were males; but in a hundred other collected cases fifty-three males and forty-seven females were found. Rischbieth and Barrington in 126 cases found seventy females and fifty-six males.

Pathogeny.—Various hypotheses have been propounded. It has been thought that the condition is a sudden alteration in type of the species—a reversion to the ancient pygmies (Apert.) Several writers have considered that achondroplasia is the outcome of a maternal toxæmia, which acts on cartilage either directly, or indirectly through the ductless glands, or through the nervous system. Shattock regarded it as a para-cretinoid state, Baumel and Margarot as due to partial insufficiency of the anterior lobe of the hypophysis; Crew takes the same view; and Parhon and Schunda as the result of hypersecretion of the gonads and insufficiency of the thyroid, pituitary, and possibly thymus. A cretinoid form of achondroplasia with modifications of the soft tissues and changes in the thyroid has been described by Symmers and Wallace. There is no evidence that it is caused by tuberculosis, syphilis, alcoholism, or consanguinity in the parents. Disease of the placenta has been recorded in a few instances and it has been argued

that achondroplasia is due to high amniotic pressure (Jansen), but this has not been proved. The disease may not be invariably congenital, for in rare instances it has been noted to begin after birth (Schorr). The relation of the disease to rickets has been much discussed, and formerly the condition was called fœtal rickets.

Parsons believes it is related to other forms of chondrodysplasia and he would regard achondroplasia as the extreme example of dysplasia—aplasia of the growth cartilage. Bauer considers the disorder in the light of a constitutional anomaly preventing normal cell proliferation of the epiphyseal cartilages, the cells being hypoplastic in various degrees, sometimes more severely, and showing irregular arrangement or mucoid degeneration, the latter being observed usually in the non-viable new-born. Bauer considers growth is a complex biological unit represented in the germ plasm and that it cannot be pure coincidence that in a family achondroplasia, dwarfism, general or partial gigantism, and acromegaly, occurred in the several members. Brailsford records an interesting atypical achondroplasic family.

Morbid anatomy.—(1) In stillborn achondroplasics the long bones (except the clavicles, which are usually normal), especially the humerus, femur, tibia, and ulna, are shortened, sometimes to half their normal length ; the shafts are firm, show excess of perio-osteal bone (periosteal osteogenesis is normal), and instead of being smooth present prominent ridges for the attachment of muscles. The normal curves of the bones are exaggerated, and symmetrically so ; the diameter of the bones is about normal, but the medullary canal may be obliterated. The tibia is usually shorter than the fibula. The epiphyses, though apparently enlarged, are of normal size (Dixon), but the shortening of the shaft produces a striking deformity which has been compared to an hour-glass (Emerson). They are usually vascular and may be soft. Fusion with the shaft may be much delayed. The diaphyses of the long bones are expanded at their ends, and fit in a cup-like manner over the epiphyses ; this accounts also for the beading of the ribs. In X-ray pictures, in addition to the above, a characteristic feature is the appearance of the epiphyseal centres of ossification much closer to the ends of the respective diaphyses than in normal bones. The joint space therefore appears to be much increased in width. The skull is enlarged, suggesting hydrocephalus, which according to Dandy is common, though not progressive ; the fontanelles may be widely open, and there are bosses on the frontal and parietal bones. The most important change is synostosis of the basi-sphenoid and occipital sutures, which leads to shortening of the base of the skull and to a rigid, funnel-shaped foramen magnum which is diminished in size. The pituitary fossa is also smaller than usual. The viscera and the thymus and thyroid do not show any constant changes. The skin may be thickened. Hydramnios may occur. Gilmour, in five achondroplasic stillborns, found excessive hæmopoiesis in the liver and he suggests that this may be related to the reduced space available in the short bones. In an achondroplasic infant which lived for six weeks there was no hæmopoiesis in the liver.

(2) In older achondroplasies the changes are on the same lines as in the newly born. The long bones of the limbs, especially the humerus, are short, but the clavicle is as long as the radius. The scapula is dwarfed, and the glenoid fossa is proportionately too small for the head of the humerus. Two groups of cases have been described on the basis of the state of the epiphysis : (*a*) those in which union with the shaft is much delayed, so that it is still ununited in middle life ; and (*b*) those in which ossification is unduly advanced but in both instances dwarfing of the

FIG. 477.—ACHONDROPLASIA, AGED FIVE YEARS.

bone results. The pelvic bones appear to be broader and stronger than normal, but the true pelvis appears to be generally contracted (Brailsford). The sacral promontory projects into the pelvis and narrows the true conjugate which is seldom more than $2\frac{3}{4}$ inches. The vertebral bodies in the dorso-lumbar region may be wedge shaped ; this may range from a slight to a more marked degree (Romanus), and sometimes a moderate kyphosis is seen.

MORBID HISTOLOGY.—The microscopical changes in the epiphyseal cartilages are the essential feature of the condition. There is aplasia

of chondral ossification. The cartilage is strikingly abnormal, the cells are few and irregular, and the inter-cellular substance fibrous or fibrillary. The cartilage is vascular, and is vacuolated by the numerous vessels. A most important change is the presence of a transverse layer of vascular fibrous tissue which passes in from the periosteum, and divides the zone

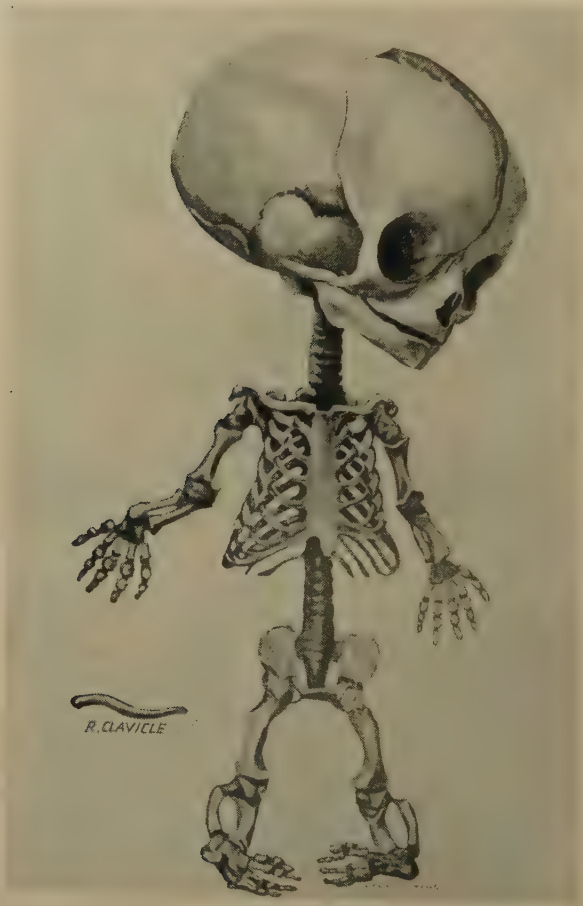

FIG. 478.—DRAWING OF SKELETON OF ACHONDROPLASIC INFANT (ST. GEORGE'S HOSPITAL MUSEUM).

Notice the trident hands and the shortening of the long bones except the clavicles, which are normal.

of ossifying cartilage from the remainder of the epiphyseal plate. Kaufmann describes three forms of achondroplasia, which may all be found in the same individual, though one usually predominates: (1) hypoplastic, in which proliferation of the cartilage cells is diminished and their columnar arrangement defective, the epiphyses being of normal size; (2) hyperplastic, with excessive proliferation of the cartilage cells

and defect in their columnar arrangement, the epiphyses being enlarged; and (3) malacia, with softening of the cartilage, defective columnar arrangement of the cells, and a gelatinous and vascular matrix.

Clinical picture (fig. 477–479).—The most striking feature is the contrast between the stunted limbs and the trunk, which is normal in length, though narrow. Hence the shortness of the body as a whole is not so obvious in the sitting posture. The hands may not extend below the great trochanters, and from the shortness of the lower extremities the subjects can often, when standing, stoop down and kiss their toes.

FIG. 479. ACHONDROPLASIA.

The shortening of the limbs (micromelia) is greater in the proximal segment (for example, the upper arm) than in the distal segment (such as the forearm); this is spoken of as "rhizomelic micromelia." There may be furrows around the limbs as if the soft parts were too large for the bones, and the transverse diameter of a segment may almost equal its length. The muscles of the limbs are well developed, the strength is often above the average, and the subjects resemble small athletes.

In the erect position the buttocks are prominent, and there is lordosis. The gait is waddling, and walking is often a late accomplishment. Amusement may be caused by the peculiar way in which the child rises from the lying-down to the erect position—the shortness and power of the legs allow of this without the use of the arms.

Kyphosis and scoliosis are rare complications. The pelvis is smaller in all diameters; so the sacrum is tilted and this further reduces the conjugate measurement. The long bones which are stunted and thick, may show sharp curves at the junctions of the shafts, and epiphyses. Thus bow-legs and apparent genu retrorsum are common. The head of the fibula is much nearer to the knee-joint than normal; this is a persistence of the normal condition of the eighth month of intra-uterine life. In some cases extension at the elbow is restricted (Turner); in others there is hypotonia. The hands are broad and very short, and the fingers, which are also short, thick, and somewhat conical, diverge from each other, the index and middle fingers being deflected to the radial side, and the ring and little fingers to the ulnar. This appears to be due to enlargement of the heads of the proximal phalanges. This condition, which recalls the spokes of a wheel, has been called the

"trident hand," and compared by Thomson to the shape of the hand in some gorillas. In some cases the fourth digits are much shortened, as the result of dwarfing of the fourth metacarpals and metatarsals, but this localized dyschondroplasia (Robin and Weill) is not peculiar to achondroplasia (Chevallier).

The head is brachycephalic, relatively large, and the frontal region bulbous; the chin and lower jaw are well developed and the lips are thick, but the face is small and the root of the nose is depressed. At birth the face has a cretinoid aspect, but it is that of an adult, not of an infant, cretin. The tongue often projects from the mouth at birth, but this is not noticeable later.

Dentition begins at the normal time. Mentally achondroplasics are generally well up to the average, and quite clean, but in some instances a form of mental weakness, which is peculiar in being accompanied by love of relations, has been described (Zosin). Achondroplasic dwarfs often show marked signs of hypergenitalism, the secondary sex characters are very well developed. The puberal changes take place at an early age and sexual activity may become particularly high (Hauer). Cæsarean section has been performed four times on the same achondroplasic woman (Frühinsholz and Michel). Affected girls are often obese, but boys are rarely so. The abdomen is prominent, and, owing to the shortness of the legs, the umbilicus is below the middle point of the body. Inguinal hernia is not uncommon. Blood phosphatase shows low normal limits.

Prognosis.—Many achondroplasics are stillborn, dying at the eighth month of intra-uterine life. A considerable number are born prematurely, and die soon afterwards, death being probably in most instances connected with the narrow, rigid foramen magnum and the resulting pressure on the spinal cord. From general œdema or ascites there may be great difficulty in the birth of achondroplasic infants. In achondroplasic mothers the difficulty of delivery may lead to the death of the offspring. When the achondroplasic survives the first year of extra-uterine life, the disease does not shorten life, except in pregnant women. The prognosis as to growth is bad; the height is not likely to exceed four and a half feet.

Diagnosis can be made at a glance by recognizing that the dwarf has a trunk of normal dimensions with extremely short limbs (micromelia) but considerable variation in the degree of limb shortening, as between the upper and lower limbs, may be noted in a series of cases (Neale, 1951).

Differential diagnosis.—This has to be made from cretinism. In a true cretin there are no marked facial changes at birth, no prominence of the buttocks, and no want of proportion between the trunk and the limbs. In achondroplasics the thyroid is usually palpable, there are no supraclavicular pads of fat, and in older ones the mental and sexual characteristics are normal.

Difficulty may also be experienced with rickets. Achondroplasics erupt their teeth normally, their general health is good and they do not present any rickety deformities. But it must be remembered that rickets may complicate achondroplasia. Dwarfs are small in all dimen-

sions, and their proportions are normal. Achondroplasics are deformed dwarfs, the limbs being unduly short as compared with the trunk. This same difference holds good between achondroplasia and the various forms of infantilism, and it is generally possible to find a cause for the infantilism. In osteogenesis imperfecta the ossification of the membrane bones of the cranial vault is delayed and deficient, whereas in achondroplasia it is normal.

Méry and Babonneix described as hyperchondroplasia or the converse of achondroplasia, the changes of elongation and thinning of the long bones of the extremities. X-ray examination showed that the epiphyseal cartilages were perhaps more developed than normally. Marfan had previously described this case, apparently unique, as one of "dolichostenomelia."

Treatment.—Thyroid treatment has been tried without benefit. Shechter recorded some remarkable effects of a pituitary growth extract, including a case of an achondroplasic girl, aged six and a half years, who grew $1\frac{3}{4}$ inches in eight months, together with a change in facies and less bossing. No further favourable experiences of this form of treatment have been reported. Osteotomy for correction of the bow-legs may be justifiable, but is very rarely necessary.

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Punctate Epiphyseal Dysplasia

Synonym.—Chondrodystrophia calcificans congenita (Raap).

In this condition there are shortened limbs, especially the upper arms, and flexed joints but the epiphyses shows generalized stippling which on microscopic examination reveals mucoid degeneration of the chondrium

of the cartilaginous matrix. X-ray pictures (fig. 480 and 481) show humeri mushroomed at both ends and the epiphyses stippled, and the shafts short. The femoral necks are abnormally ossified. There is also stippling of the other epiphyses especially those of the tibia and pelvis. The disorder has been recognized usually in infants. The infant may be

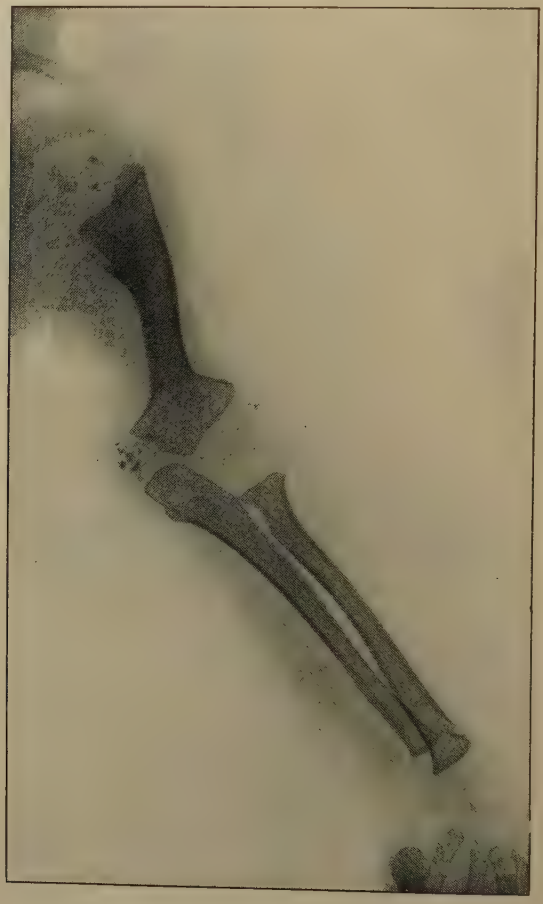

FIG. 480.—PUNCTATE EPIPHYSEAL DYSPLASIA—UPPER LIMBS.

The humerus is short with splayed ends and epiphyseal stippling. There is an old fracture of the humerus.

relatively immobile, the knees flexed and resistant to extension and the upper arms short. Congenital cataract or congenital heart disease may also be present. Borovsky (1944) observed that, apart from stippling at many epiphyseal centres, there may be extensive calcification around the knee-joints and possibly periosteal elevation along the femur. The calcific deformity would therefore appear to be not entirely confined to the epiphyses. No evidence of any endocrine deficiency has been

found in this disease. The serum phosphatase is considerably raised. In several instances two or more examples of the disorder has occurred in the same family. The prognosis is uncertain but Raap considers that

FIG. 481.—PUNCTATE EPIPHYSEAL DYSPLASIA—LOWER LIMBS.
The short femora have splayed ends and stippled epiphyses.
(By kind permission of Dr. Reginald Lightwood and the *Proc. roy. Soc. Med.*)

the abnormal calcifications are most marked at birth and may disappear by the age of three years; in Borovsky's case skiagraphs taken at one year of age showed almost complete absorption of the calcium deposits at the knees and the appearance of normal bone formation in some of

the stippled areas. The viability of these infants appears to be inferior; two personally observed cases have died under the age of six weeks.

Treatment is essentially concerned in mild cases to prevent contractures. Normal dosage of vitamin D is not contraindicated by the abnormal calcification.

Epiphyseal dysgenesis may be associated with cretinism or hypo-

FIG. 482.—CRETIN (UNTREATED), AGED TWO AND A HALF YEARS.

The following may be noted: (*a*) Linear markings lower ends of femoral shafts; (*b*) Density at the epiphyseal lines; (*c*) Absent upper femoral epiphyses; (*d*) Fragmented lower femoral and tibial epiphyses. (Case of Dr. Braid's.)

thyroid disorder and was found in twenty-three of twenty-five hypothyroid children by Wilkins. This particular change in epiphyseal development may be widespread in the patient and appears radiologically as a mottled form due to irregular islets of ossification which eventually form a porous spongy mass (fig. 482). The dysgenesis is found most frequently in the head of the femur and treatment of the hypothyroid state with thyroid extract enables ossification to proceed more normally.

Epiphyseal mottling or fragmentation may be seen in some of the epiphyses in the Brailsford-Morquio type of deformity.

In osteopetrosis a suggestion of stippling may be seen in some of the epiphyses. Mottled epiphyses in a case of pituitary gigantism is described by Traub.

Fairbank (1945) under the title "dysplasia epiphysealis multiplex" describes a developmental error characterized by dwarfism, stubby digits, and mottling or irregularity in density and outline of developing epiphyses. In fourteen cases the ages varied from eighteen months to twenty years. It affects both sexes and may be familial. Flexion contracture or limited movement of some of the joints may be present. Difficulty in walking, due to pain and stiffness, especially of the knees, may occur. The pathology is obscure. X-ray pictures show the epiphyses to be late in appearing, backward in development and irregular in ossification, giving a mottled appearance and peripheral stippling. The tendency is towards improvement in epiphyseal density, but the outline and some permanent deformity may remain in the hips, shoulders, ankles, or knees. The head of the femora or humeri may remain shallow and less convex. The shafts are shortened, but usually not thickened. The vertebral bodies are not abnormal. An extended discussion is given by Fairbank (1951) on this group of abnormalities, and a representative case is described by Buxton.

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CRANIAL ABNORMALITY

The almost infinite number of minor variations in the form of the human skull normally calls for no special comment and even within the same family head shape is often quite different. However, limits of normal anatomical variation are accepted although some gradation into the descripitive abnormal types is evident. Several classical forms of cranial dysostosis with or without associated abnormalities elsewhere in the body, have been defined, and possess descriptive names: hypertelorism; oxycephaly; scaphocephaly; craniofacial dysostosis; cleidocranial dysostosis; cranio-carpo-tarsal dystrophy; leontiasis ossea; and gargoylism. The wider aspects concerning genetics are considered by Neale (1951).

It is of great interest and of some importance that gross deformity of the skull, such as acrania, anencephaly or hydrocephalus, and certain

other conditions, *e.g.* achondroplasia, cranio-cleido-dysostosis, cranio-facial dysostosis, and lacuna skull can be identified radiologically in the fœtus *in utero* (Brailsford, 1944).

Premature synostosis causes alteration in the skull outline. *Oxycephaly* (fig. 483) (turricephaly) is indicated by an abnormally high and thin skull in which the frontal bones are fused and convolutional impressions are present. In *scaphocephaly* (fig. 484) there is a long antero-posterior

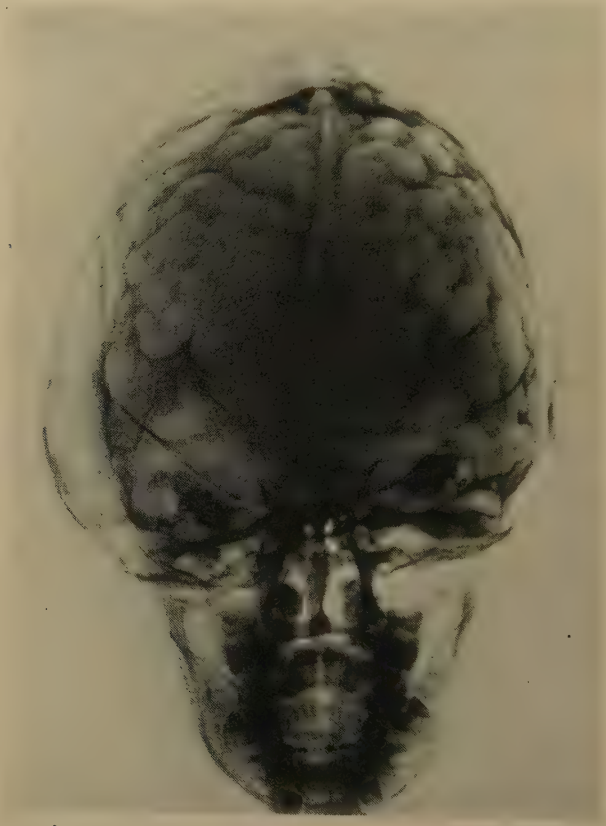

Fig. 483.—Oxycephaly.

diameter and some smallness in size. *Plagiocephaly* is an asymmetrical form of craniostenosis and the contrast is marked between the compensating overgrowth and bulging of the segments which have not fused and the limited growth of the other. Premature fusion of the frontal bones produces *trigonocephaly* in which the anterior part of the skull is keel-shaped with some compression of the anterior fossa, the orbits and ethmoid bones and some compensating bulging of the posterior segments of the skull; obstetrical difficulty may occur from this. In the micro-cephalic skull in which the brain is small, there is early closure of sutures and a convex upper border of the floor of the anterior fossa.

In achondroplasia the premature synostosis of the bones at the skull base and the synchronous bulging of the membrane bones has been already described. Rarely, in chondrodysplasia, some faulty ossification may occur at the base. In osteopetrosis the bones of the skull may show thickening and increased density and the basal foramina diminished in size. A thin shell of bone with defective areas is seen in osteogenesis imperfecta. In fibrous dysplasia of childhood the skull becomes remarkably thick and the head appears large and rather like adult Paget's disease. Arachno-dactyly is associated with cranial deformity. Sub-

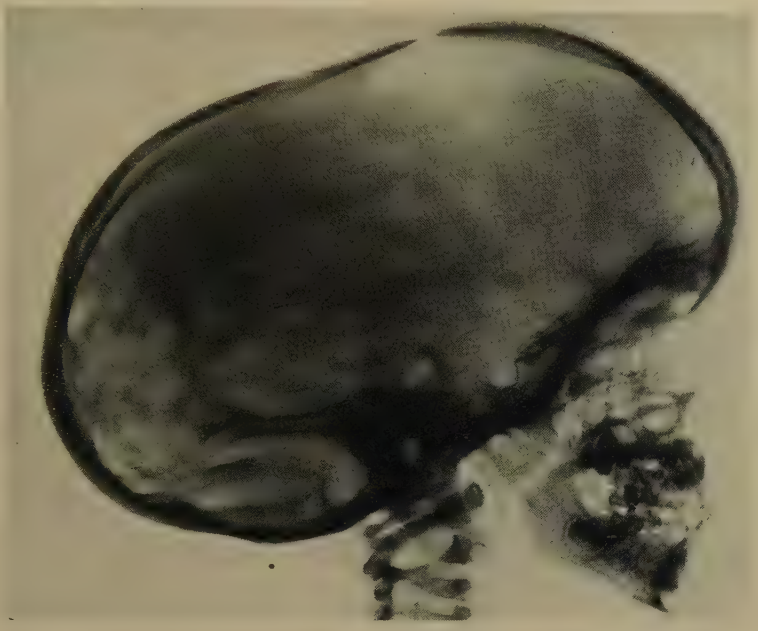

Fig. 484.—Scaphocephaly.

aponeurotic hæmorrhage followed by calcium deposit may supervene in scurvy. In severe degrees of rickets the bones of the head are rarefied and the denticles prominent in contrast. In renal rickets the woolly skull due to decalcification changes is observed. Some forms of chronic erythroblastic anæmia (Cooley) shows characteristic changes in the bone appearances of the skull.

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Oxycephaly

Synonyms.—Acrocephaly, Acrobrachycephaly, Tower head, Steeple skull.

In this remarkable deformity of the skull, due to fœtal synostosis of the sutures, the head is abnormally tall, broad, and short from before

backwards (brachycephaly), there is exophthalmos, the palpebral fissure is oblique, the external canthus being at a lower level than the internal. Virchow in 1851 stressed the early closure of the cranial sutures and von Graefe in 1866 described concomitant visual defect. The oxycephaly is often accompanied by more or less obvious bony deformities, especially union of the digits of the hands and feet, called by Apert, acrocephalo-syndactyly (fig. 485). Park and Powers, who have collected twenty-nine such cases and believe that the cranial and limb deformities are more often associated than is usually believed, inclined to the view, based on their belief of its familial nature, that this condition is due to a defect in the germinal plasm. The recorded cases appear to be chiefly isolated, but it may be transmitted from a parent to one or more children and even to a third generation. In scaphocephaly, in which from fœtal synostosis of the sagittal suture the skull is much elongated, deformities of the hands and feet have been much less often recorded. Greig describes three forms: (1) true oxycephaly present at birth and due to general craniofacial synostosis and often associated with syndactyly and allied deformities of the extremities; (2) delayed oxycephaly due to premature cranial synostosis, and not associated with deformities of the extremities; and (3) false oxycephaly due to localized synostosis during cerebral growth, and often of a recognizable origin. Boys are more often affected than girls.

FIG. 485.—ACROCEPHALO-SYNDACTYLISM, AGED SIX WEEKS.

Morbid anatomy.—In true oxycephaly there is universal synostosis of the cranial and facial bones; the accessory nasal sinuses are rudimentary or absent, and the maxillæ undeveloped. The skull is cone-shaped, the apex being in the position of the anterior fontanelle. The skull is thinned in places, and may show a marbled appearance, the "digital" markings. The forehead is vertical, the orbits shallow, and the hard palate narrow. In true oxycephaly the growth of the brain is often inhibited.

Clinical picture.—In addition to the lofty skull and exophthalmos, the facial appearance is somewhat suggestive of chronic nasal obstruction. There is usually nystagmus and the protrusion of the eyes may become so extreme that the globe is dislocated. Raised intracranial pressure is present. Headache is common, impairment of the senses of smell and hearing, and loss of vision from optic atrophy may occur, but mental

processes are usually unaffected. The condition must be distinguished from hydrocephalus. X-ray examination of the skull shows convolutional atrophy and no trace of the sutures.

Treatment.—Headache may require symptomatic treatment and in cases of increased intracranial pressure causing optic atrophy decompression should be considered. Cruciform linear craniotomy might merit consideration.

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Cleido-Cranial Dysostosis

First described by Morand in 1766, then by Sir Thomas Barlow in 1883, this condition did not attract any attention until Marie and Sainton gave it the above name in 1898. In 1894 Marie and Sainton presented a father and son both showing similar abnormalities, namely, the fontanelles had failed to close, the superior maxilla was retracted on the lower jaw, the teeth were of poor shape and irregularly placed, the palatine arch was curved and only partially fused in the median line, the clavicles were reduced to a sternal and an acromial portion, the mid-part being absent. A year later, a mother and daughter presented similar anomalies. Because of the similarities Marie and Sainton finally concluded that a special name was necessary and they proposed " dysostose cleido-cranienne héréditaire," which described succinctly the basic characteristics of the disease.

In 1905 Villaret and Francoz tabulated forty-five cases, and in 1910 Fitzwilliams analysed sixty cases. Fitchet, reviewing the whole subject in 1929, suggested the above title was inaccurate, since the only constant abnormality was cleidal dysostosis, which, though always congenital, was not invariably hereditary, and might occur without other abnormalities.

Definition.—Congenital absence or imperfect development of the clavicles usually associated with deficient and defective ossification of the vault of the cranium and other abnormalities.

Ætiology.—It is often hereditary and several members of a family suffer. Thus in Fitzwilliams's series eight families provided thirty-one examples, and in the family described by Langmead cases occurred in four generations. Incomplete forms occur, especially in affected families. Fitchet found six examples in three generations ; in three of these cases the right clavicle only was affected. It can be transmitted both by the mothers and by the fathers. Sex does not exert any influence ; in fifty-four cases there were twenty-eight females and twenty-six males (Fitzwilliams).

There is no convincing evidence that consanguinity of the parents, tuberculosis, syphilis, rickets, or various infections or intoxications are responsible. The developmental defect begins early (second month) in fœtal life. Jansen attributes it to excessive amniotic pressure acting particularly about the eighth week. It has been suggested that it is a partial and hereditary variant of osteogenesis imperfecta (Durante).

Pathogeny.—Nothing is really known, but several hypotheses have been put forward. It has been thought (1) that the causal factor of the maldevelopment of the membranous bones is deficiency in some chemical constituent (Fitzwilliams); (2) that the condition is a reversion to the type of animals without clavicles, such as the cetaceans, or to the type of animals with rudimentary clavicles, such as the carnivora; (3) that it is an example of an abrupt variation in the human type termed "mutation" by Vries.

Morbid anatomy.—Clavicles.—Both may be completely absent (six out of sixty cases); it is rare for one clavicle only to be absent or deficient (see above). More often the sternal end is present and the rest of the clavicle is absent, the sternal end having a ligament attached to it, which is thought to be the costocoracoid membrane. In rare instances the sternal portion is absent and the acromial end present. In a considerable number of cases the sternal and acromial ends of the clavicle are both present, but not united so that there is a congenital pseudo-arthrosis. The condition of the muscles attached to the clavicle—the subclavius, the sterno-cleido-mastoid, the trapezius, pectoralis major, and deltoid—naturally varies with the state of development of the clavicle; thus the clavicular portion of the trapezius is often absent.

The skull.—The defective development of the membrane bones leads to large anterior and posterior fontanelles, or to the presence of one large fontanelle. Closure is long delayed, and though usually complete at the age of twenty, may not occur at all. The parietals may be found completely unossified. The biparietal diameter is increased, and the vertical and fronto-occipital diameters are diminished. Apparently as the result of an attempt to compensate for the deficient ossification, bosses are formed over the frontal, parietal and occipital bones—three on each side, so as to produce a hot-cross bun or natiform skull. The growth of the superior maxillæ is interfered with, and the palate is highly arched and sometimes cleft. This stunting of the facial bones is secondary to maldevelopment of the cartilaginous base of the skull (Fitzwilliams). The frontal sinuses are exaggerated, whereas the sinuses of the face are diminished in size. According to Muchet, anomalies of the teeth are almost constant, the first dentition is delayed, and often persists to the twelfth year; some teeth, especially the upper incisors, are missing; the teeth are small, irregular, badly embedded and become carious early and rapidly. Millhon and Austin, in a recent review, also consider that the dental findings in these cases are almost constant. The deciduous teeth erupt normally, and are retained longer. The permanent teeth may lose their eruption stimulus and stay embedded in the jaws. Later resorption of the alveolar ridge may occur and the embedded teeth near the surface

come into view. The high incidence of supernumerary permanent teeth, as well as the common occurrence of geminated teeth, is another of the dental peculiarities found. If there are many teeth present in the jaws, the alveolar ridges are quite thick and the gums appear hypertrophied. The maxilla is undeveloped in comparison with the mandible ; the roof of the mouth has a tendency to be narrow and high, and the mandible, although apparently complete in development, and normal in size, appears to be prognathous.

Other bony deformities, such as scoliosis, lordosis, kyphosis, defects in the shape of the sternum, and dwarfing of the little finger may be present. X-ray examination has revealed absence of ossification in the pubis, carpus, and os calcis, epiphyses at both ends of several metacarpals and phalanges, and the infantile type of coxa vara (Barrington-Ward and Fairbank).

FIG. 486.—BOY WITH HEREDITARY CLEIDO - CRANIAL DYSOSTOSIS (VILLARET AND FRANCOZ).

Clinical features.—The patients, who are usually short in stature and may be somewhat fat, are often unaware of their deformity, which is naturally much more obvious in thin, than in fat, subjects. Their undue mobility allows the shoulders to be brought in contact under the chin (fig. 486 and 487). The head is enlarged, the forehead bulging, with a depression between the frontal bosses, but the face is small ; the supra-orbital ridges are prominent, and from depression of the roof of the orbit there may be some exophthalmos, so that the general aspect resembles that of slight hydrocephalus. As a rule the mental faculties are normal and the general health good. Incomplete forms of the condition are not uncommon.

Diagnosis.—This depends on the association of defective development of the skull bones formed in membrane, and of the clavicles. It must be distinguished from intra-uterine fracture of the clavicle.

No **treatment** is necessary apart from possible dental attention.

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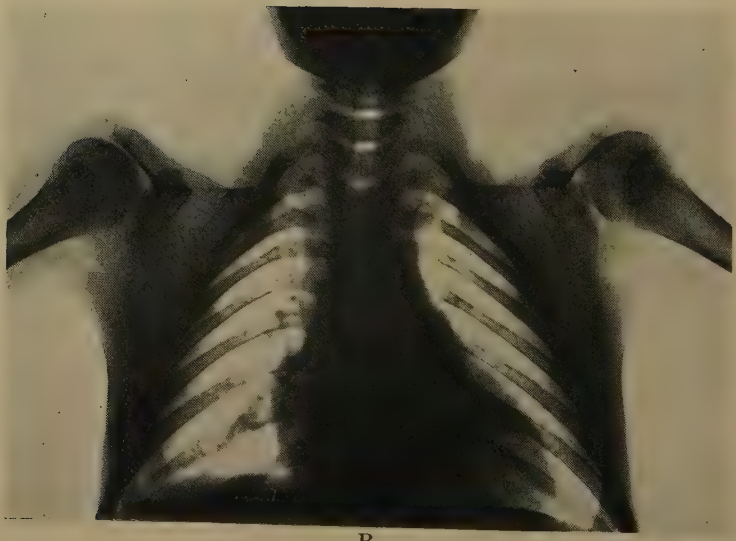
A



B

FIG. 487.—CLEIDO-CRANIAL DYSOSTOSIS.

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Hypertelorism

This name has been given by Greig to a congenital cranio-facial deformity the main feature of which is the excessive width between the orbital fossæ (fig. 488). Many of the cases reported since Greig's original article are obviously below the average in mental capacity, but some of them appear to be of normal mentality. Many of them have further abnormalities in the development of the bony skeleton. Reilly, in 1929, reported four cases making a total of seventeen published at that date. The characteristic facial appearance is attributed by Greig to an abnormal development of the sphenoid bone, resulting in an overgrowth of the lesser wing of this bone, and an undergrowth of the greater wing. The result of this error is to thrust forward the whole frontal bone, and separate the nasal bones more widely than normal; thus characteristic facies are produced. The remaining skull bones may or may not be altered in their mutual relationships depending upon the degree of malformation of the sphenoid. Cleft palate was present in a case reported by Bett. Lightwood and Sheldon reported a unilateral case.

Fig. 488.—Hypertelorism. (Prof. Parsons's Case).

There is evidence that this maldevelopment tends to be an inherited characteristic. Abernethy has recorded its appearance in four generations.

In the rare examples of central hare-lip with cleft palate there is usually an associated degree of hypertelorism, and in some such cases a basal encephalocele can sometimes be detected, protruding through the cleft in the palate (Oldfield).

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Lacuna Skull

Hartley and Burnett (1943) have recorded the characteristic skull changes under the terms craniolacunia and craniofenestria. These

peculiar aberrations of cranial ossification occur in the membrane developed bones, especially the frontals and parietals, but the condition may be seen also in the squamous temporals and membranous part of the occipitals and occasionally in the greater wings of the sphenoid.

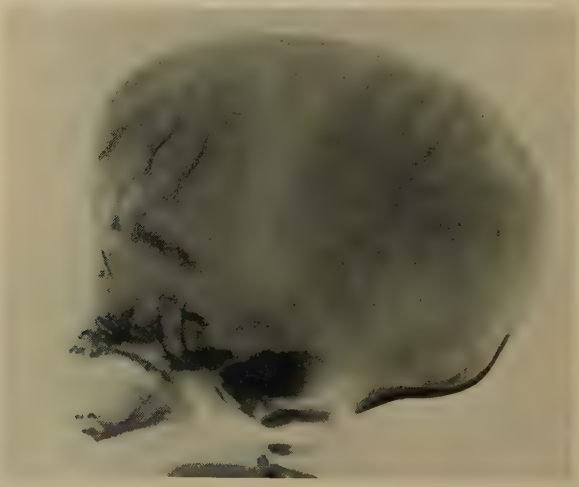

FIG. 489.—RADIOGRAPH OF SKULL AT BIRTH SHOWING CRANIOLACUNIA.

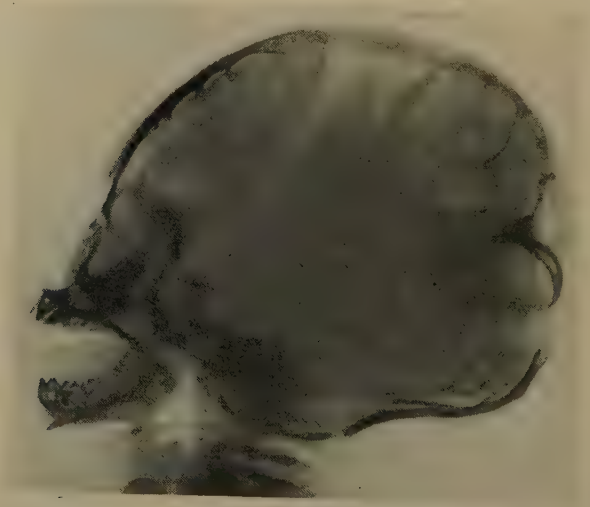

FIG. 490.—RADIOGRAPH OF SKULL AT BIRTH SHOWING CRANIOFENESTRIA.
(By kind permission of Drs. Hartley and Burnett, and the *Arch. Dis. Childh.*)

Craniolacunia is essentially shown as circular or oval thickenings on the inner surfaces of the skull and a corresponding thinness of the bones inside the thickened bars. In craniofenestria the ossification between the thinned areas is even more defective, so much so that actual absence or

almost complete absence of bone is noted in some areas between the dense ridges. The outer surface of the skull is normal except where there is bone absence in the fenestrated skull. The bones affected may be reduced in weight by 70 per cent. The edges of the bone are irregular. The bony bars themselves may be of considerable thickness, exceeding the thickness of the normal skull for the same age. The two degrees of the skull disease can be detected by skiagram examination *in utero*. On ante-natal radiography the defective ossification of the vault is looked for and at the same time other defects may be recognized, *e.g.* spina bifida or hydrocephalus; but it may be detected irrespective of the size and shape of the skull. Craniostenosis may be evident. At birth the defective outline of the vault is confirmed radiologically and in craniofenestria there may be projections visible beyond the outline, and the bars form a coarse reticulation. Extreme degrees of craniofenestria may occur in various sized skulls—microcephalic, hydrocephalic or normal—and the mildest form of craniolacunia may also be seen. Study of the dried vault bones reveals bony bars on their inner aspects whilst lacunæ are numerous. Even with the dense bars of craniofenestria the weight of the bone may be only about 25 per cent. of the normal (fig. 489 and 490).

When craniolacunia occurs unassociated with other body defects it tends to become less apparent, although it remains somewhat identifiable, and so may be recognized in the parents or relatives of infantile cases. It appears that craniolacunia or fenestria are probably developmental anomalies similar to spina bifida and occurring usually in association with it, but also separately. Leeuwen's case is an excellent example of the associated cranial and spinal abnormalities. Defective formation of the mesodermal tissues surrounding the neural plate would seem to be operative. The spinal defect may vary: spina bifida oculta, myelocele, myelomeningocele, or syringocele. Hartley and Burnett consider that all cases of spina bifida should be skiagraphed for evidence of lacuna skull. They estimate that the incidence rate of this distinctive developmental anomaly of the skull may be nearly 1 per cent. of all births. The frequent association with spina bifida should be recognized, and in fact possible laws governing the inheritance of spina bifida might be discovered indirectly through greater attention to the incidence of craniolacunia and craniofenestria.

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Hereditary Cranio-Facial Dysostosis

Crouzon in 1912 described this syndrome and depicted certain features. These included oxycephalic cranium, marked atrophy of the superior maxillæ and absence of their sinuses, atresia of the nasal fossæ and a parrot beak-shaped nose and marked exophthalmos (fig. 491). Divergent squint, primary optic atrophy and occasional nystagmus and coloboma

of irides may be present. The palate is high arched. It is hereditary and familial. X-ray examination shows a dome-shaped malformation

FIG. 491.—CRANIO-FACIAL DYSOSTOSIS.

of the vault, obliteration of osseous sutures, thin skull with digital impressions and sinking in of the middle fossa and a nearly vertical position of the sella. The condition may be considered to be a variant of the oxycephalic group.

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Cranio-Carpo-Tarsal Dystrophy

In 1938, Freeman and Sheldon recognized an undescribed clinical entity and gave it the above name. The two children were under three years of age and unrelated, but looked very similar. Parents were healthy.

"The lower forehead and eyebrows were occupied by a soft prominent transverse swelling and the eyes were buried so deeply that they were hardly visible. The nose could barely be recognized, the nasal openings were small, and the mouth was small. The hands showed ulnar deviation and the feet a severe degree of talipes equino-varus."

The eyes appear more widely separated than normal and the nasal bridge broad. Both cheeks are abnormally fat, rosy and shiny. "The

part of the face below the eye appears too small in proportion to the forehead." X-ray examination of the skull shows a steep sloping anterior fossa, and abnormal and partial failure of union of the frontal bone with the floor of the skull. There are fortunately no bony changes in the hands or feet. Orthopædic treatment proved beneficial.

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SKELETAL DEFECTS

Klippel-Feil Syndrome

Congenital anomalies at the lower end of the cervical spine occur and similar changes in the upper dorsal, resulting in shortening and limitation of movements of the neck. Klippel and Feil described the deformity in 1902. The baby is often wizened and the head is tilted upwards and backwards (fig. 492). There is an occipital prominence with a spur of bone in the mid-line. The cervical and dorsal spines are usually not palpable and the scapulæ are winged. There is bilateral web-neck and some degree of torticollis. Head movements are limited and the chin is hypognathous and pointed. A thick growth of hair extends down the neck. Scoliosis of the dorsal spine and deformity of shoulder may be seen. Progressive spastic paralysis of the upper and lower limbs often occurs and muscular contracture of the hands and feet. X-ray pictures may show multiple hemi-vertebræ in the cervico-dorsal junction or synostosis of the upper vertebral bodies and arches and possibly failure of fusion of the arches in the lower cervical and upper dorsal region. Occasionally cleft palate or hare-lip is also present.

FIG. 492.—KLIPPEL-FEIL SYNDROME, AGED TWO WEEKS

REFERENCE

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Arachno-Dactyly

Synonyms.—Hyperchondroplasia, Spider Fingers.

This condition was first described by Marfan, who called it dolichostenomelia. Achard suggested the name arachno-dactyly.

Pathogenesis.—Ormond and Williams incline to the view that it is a developmental abnormality and not of endocrine origin, and this is supported by Lutman who found, in a kinship of forty persons, seventeen members with Marfan's syndrome. A great deal of variability was apparent in the various defects, so much so that some would be unsuspected were it not for their genetic background.

Clinically the digits of the hands and feet are peculiarly long and slender, and the bones of the limbs show the same characters (fig. 493). Epiphyses may occur at the distal and proximal ends of the first and second metacarpals and metatarsals and for all the proximal and distal phalanges. The muscles are small and weak, and the joints are flexed and their movements restricted. Out of seventeen collected cases nine at least had ocular symptoms, such as congenital dislocation of the lens with concomitant trembling irides (Ormond and Williams). Prominent supra-orbital ridges, and hypertrophied ears may be recognized. Congenital heart disease is not infrequently present. Associated amyoplasia congenita has been recorded by Mackay. The mental state is normal.

The children with this obscure congenital abnormality are slender in build and may have kyphosis, and are so muscularly weak, with evident hypotonia, that they are prone to succumb to intercurrent infections.

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Congenital Elevation of the Scapula

Synonym.—Sprengel's deformity.

Of this condition, described by Sprengel in 1891, there are more than a hundred examples on record, but the cases described under this heading are not all of the same nature.

Ætiology.—Sprengel's view that the condition is mechanical and due to prolonged fixation of the arm behind the fœtus's back *in utero*, on account of a deficiency in the amount of amniotic fluid, is no longer accepted for in many cases the quantity of amniotic fluid has been normal. It has been thought to be due to injury during labour, or to muscular defects, especially absence of the lower part of the trapezius which allows the upper fibres of the muscle to elevate the scapula. This

(*a*)

(*b*)

(*c*)

(*d*)

FIG. 493.—ARACHNO-DACTYLY. BOY AGED THREE AND A HALF YEARS. (From *Bart. Hosp. Reports*, Vol. 53, 1920.)

defect, however, is not constant. Another view is that the scapula is malformed and abnormally situated as a result of congenital malformation involving the cervico-scapular region and upper ribs, the scapula retaining its fœtal position in the neck. In some instances, as first recorded by Willett and Walsham in 1883, the vertebral border of the scapula is united to the spine of the seventh cervical or first dorsal vertebra by a bridge of bone or rod of cartilage which has been regarded as a reversion to the suprascapular bone of lower vertebrates. In favour of the view that elevation of the scapula is a congenital malformation due to errors in segmentation of the mesoblast is the frequent presence of other abnormalities such as fusion or suppression of ribs, absence of half or whole of one or more vertebræ, polydactylism, suppression of the radius, and of the corresponding thumb (Fairbank), hydrocephalus (Nageotte-Wilbouchewitch), talipes, torticollis, local hypertrichosis (Greig), idiopathic dilatation of the colon (Boyd). Neuhof described a familial form which he regards as atavistic.

Fig. 494.—Congenital Elevation of the Scapula.

Clinical picture.—The deformity is usually unilateral, though it may be bilateral, and is commoner on the right side and in girls (fig. 494). The scapula is raised, small, and its inferior angle nearer to the spine. Absence of the lower part of the trapezius and fibrous changes in the rhomboid muscles can be detected. In cases with a bony bridge between the scapula and the spine the arm cannot be raised much above the right angle owing to the restriction of the movements of the scapula. There may be some scoliosis. Syryngomyelia was present in a case described by Critchley.

Diagnosis.—Congenital elevation of the scapula must be distinguished from elevation of the shoulder which may be due to various acquired factors, such as scoliosis. Tic of the rhomboid muscles may elevate the shoulder, and as the result of paralysis of the shoulder muscles—for example, that due to birth palsy—the scapulæ may be asymmetrical.

Treatment is hardly necessary, but exercises, massage, and surgical interference such as division of shortened muscles or removal of bony bridges, have been recommended. Removal of the bony bridge, followed by prolonged active and passive exercises, may result in definite improvement.

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Fragilitas Ossium

Introduction.—Fractures on slight provocation occur in children in various conditions, such as rickets, inherited syphilis, severe paralytic atrophy and new growth. The titles "fragilitas ossium" (fig. 495) and "osteopsathyrosis" (Lobstein, 1833) are restricted to cases in which multiple fractures without any obvious cause, either exciting or underlying, constitute the disease. The nomenclature of these cases is confusing, and it appears more satisfactory to describe two groups—(1) osteogenesis imperfecta, in which fractures are primary, and deformities and bending secondary; and (2) mollities ossium in which softening is the primary and fractures the secondary features—than to include them in one category.

Fig. 495.—Fragilitas Ossium.

Osteogenesis Imperfecta

Synonyms.—Idiopathic osteopsathyrosis, Periosteal dysplasia (Durante), Periosteal aplasia.

Definition.—A rare condition in which multiple fractures occur in intra-uterine or infantile life.

As various conditions have been grouped under this heading, a great confusion has resulted. In some cases thus described the bones are soft and pliable so that they can readily be bent (congenital osteomalacia); in others the shafts of the long bones are composed of alternate segments of cartilage and bone; and in others the bones are brittle and fracture easily. The description here will be confined to the cases showing multiple fractures. In the past it was thought that osteogenesis imperfecta was incompatible with extra-uterine life, and the cases which survived and continued to show multiple fractures were called by some other name—fragilitas ossium or idiopathic osteopsathyrosis. To cases starting in late childhood the title "osteogenesis

imperfecta tarda" has been applied by Looser. The name "osteogenesis imperfecta" was introduced by Vrolich in 1849; and the masses of callus round the fractures give rise to the misleading title "annular rickets." In 1897 Griffith collected sixty-seven cases, and in 1906, Lovett and Nichols estimated the published cases at 130.

Ætiology.—Griffith estimated that the condition was hereditary in twenty-seven per cent. of the cases. It may be met with in several members of the same family without any hereditary history. Thomson stressed the importance of the familial influence and the occurrence of blue sclerotics in the group with a post-natal onset. A study by Fairbank of twenty-eight personal cases showed, however, that though familial and hereditary influences are commoner in the post-natal than in the ante-natal cases, and though blue sclerotics are found with greater frequency in the former, there is no clear distinction between the two. In an affected family, certain members may show both brittle bones and blue sclerotics, others exhibit blue sclerotics without any bone fragility, whereas others are normal. Apparently, in an affected family, a member showing only blue sclerotics may transmit the fragility (Kersley).

Knaggs suggests the essential fault is a want of sufficient osteoblasts lining the trabeculæ and due to a fundamental error in the evolution of osteoblast. At present the precise cause of this affection is unknown.

Morbid anatomy.—In the ante-natal cases, the shafts, especially of the proximal limb bones, are short and thick, and, as a result of fractures, may show deformities and annular thickenings due to rings of callus. In those that survive, the general thickening persists at any rate for a few months. In the older case, whether ante-natal or post-natal in onset, the bones are slender and obviously poorly calcified; the cortex is thinner and less dense than it should be. Sometimes the bones show a considerable degree of honeycombing, especially in the metaphyses. The periosteum is thickened and adherent to the shaft of the bone, which has not any proper outer layer of compact bone. The periosteum of the long bones produces little true bone, but gives rise to a considerable formation of cartilage and connective tissue, whereas, in achondroplasia it is the cartilaginous formation of bone at the epiphyses which is at fault. The perichondrium of early fœtal life does not apparently undergo the normal metaplasia into the periosteum of the long bones. There is either a lack of the proper stimulus to this hyperplasia or an unknown inhibitory force acting on the osteogenetic tissues (Klotz). As already stated, Knaggs found the osteoblasts deficient in numbers, the trabeculæ of the spongy tissue of the medulla delicate and small, and the cortex of the shaft excessively thin and porous. Wyatt and McEachern found the parathyroids—three out of four—unusually vascular, with a relatively small amount of parenchymatous tissue. They suggest that osteogenesis imperfecta may sometimes be based on congenital parathyroid disturbance rather than purely the result of faulty mesoblastic differentiation. In one case the suprarenals were small (Lovett and Nichols). In an infant dying at birth the placenta was fibrous and showed areas of calcification (Klotz).

Clinical picture.—As many as a hundred fractures have been seen in a new-born child (Klotz). In Chaussier's case there were 113 fractures, seventy of which were in the ribs. The fractures occur suddenly in children, previously healthy, as the result of insufficient causes, such as muscular exertion. The fractures may be incomplete or greenstick, usually involve the shaft, but may occur at the junction of the shaft and the epiphysis.

The fractures, which are usually in the long bones and ribs, unite rapidly; the amount of callus varies much. Deformity, however, is prone to occur as the result of union; for the fractures, being due to slight injury, are less painful than in health, and may therefore, especially when numerous, escape medical attention.

Apart from the deformities due to faulty union of the fractures, mollities ossium may supervene, so that the bones bend and thus imitate the changes in rickets. In such cases the pelvis may show marked deformity (twenty-five per cent. of all cases). There is frequently deficient ossification of the bones of the vault of the skull, the bones being formed on a mosaic of small wormian bones; the temporal regions bulge, with displacement of the ears (H. C. Cameron). Electrical examination of the muscles shows a diminished response to the faradic current. In over a third of the cases the sclerotics are a deep blue in colour, a much deeper blue than that seen so commonly in normal infants. This is said to be due to diminished density of the sclerotic coat of the eyeball. It occurs in both ante- and post-natal cases, though more frequently in the latter, and may be found, without fragility of the bones, in some of the other members of an affected family. Deafness may also occur, and the combination of osseous fragility, blue sclerotics and deafness has been spoken of, by some authors, as van der Hoeve's syndrome. The teeth, particularly those of the first dentition, are much more translucent than those of normal children, and show definite evidence of imperfect calcification. As a rule the teeth of the second dentition are much better calcified than their predecessors. The involvement of this epidermal structure—enamel—in an affection of the bones and other structures of mesoblastic origin is noteworthy. Weakness and laxity of ligamentous structures has also been noted in these cases. In those who survive for any length of time, the limbs usually show gross deformity, whilst, as a rule, the spine is markedly scoliotic. Some of the milder cases display a tendency towards recovery, the fractures ceasing to recur. The blood calcium and phosphorus in these cases is normal in amount. As to serum phosphatase, Smith has found the phosphatase above normal in thirty per cent. and normal in seventy per cent. From the X-ray evidence it is possible to gain a good indication of the nature of the tissue changes and anticipate the histological structure in different sites, *e.g.* in the fœtal form the pictures show a skeleton, the elements of which have a thin shell of bone for a cortex; the internal structure showing a granular appearance indicating calcification rather than ossification; the infantile examples in some cases show, in the regions of the metaphysis, multiple, rounded, bony, cell-like structures, up to a

¼ inch in diameter, enclosing non-osseous tissue; the adolescent and adult examples show slender shafts composed almost entirely of dense compact tissue, while the expanded extremities are of a coarse cancellous tissue. Although many cases show similar progressive clinical developments X-ray photographs indicate material differences in the behaviour of the bone in others. In some, the changes are similar throughout the skeleton, usually more marked in the lower extremities, but in others may be seen a thin skull associated with changes in the bones of the hands and feet, some degree of general osteoporosis, bending and flattening of the ribs, but little else (Brailsford, 1943) (fig. 496 and 497).

Prognosis.—When fractures are present at birth, the infant, if not stillborn, will probably die soon; but in cases in which fractures do not occur until some years have elapsed there is little danger to life, although there may be much deformity. In some cases there is a marked remission of the tendency towards fracture at the onset of puberty. Deafness may make a late appearance.

Diagnosis is based on the presence of fractures at birth, or their occurrence soon afterwards on inadequate provocation. It is inadvisable to elicit crepitus, as fresh fractures may thus be induced. From rickets, osteogenesis imperfecta differs in the absence of beading of the ribs, enlargement of the epiphyses, and of the nervous and visceral symptoms.

Hyperplastic callus may occur in relation to fracture and its shape and texture may falsely suggest sarcomatous growth (Fairbank, 1948). Multiple fractures, in rare instances, occur in syphilitic infants.

Treatment.—Fractures should be treated in the ordinary way; and when union has occurred, massage and suitable exercises to obviate muscular atrophy should be employed. No benefit has followed the use of thyroid extract, calcium salts, or cod-liver oil. Gorter reported benefit from thymus; Secord considers there is some possible value in a thymus extract. Ultra-violet light has no special effect on the bones. Occasionally, in carefully selected cases, operative treatment for correction of deformities is justifiable and may be of decided benefit to the patient. There is no reliable method of avoiding the osteosclerotic deafness. In rare examples an associated avitaminosis D may be detected and some improvement occur in giving this vitamin.

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FIG. 496.—OSTEOGENESIS IMPERFECTA.

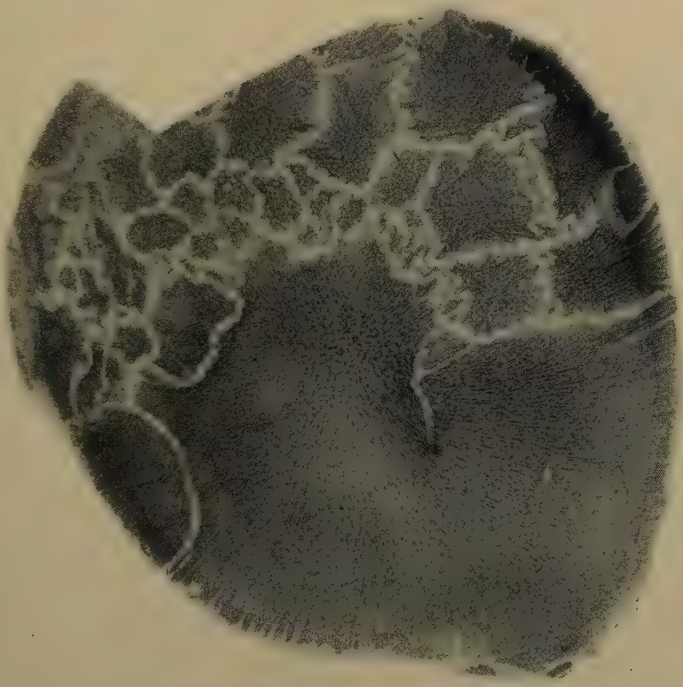

FIG. 497.—OSTEOGENESIS IMPERFECTA.
(Lower limb bones and parietal bone.)

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Marble Bones

Synonym.—Albers-Schönberg disease.

This is an entirely different affection from the above, the only symptom common to the two being the fragility of the bones. It appears to be a rare disease affecting both sexes and discovered at all ages, the ages of the recorded cases ranging from birth to seventy-five years. The feature of the disease is the great excess of lime salts in the bones. The bones in radiographic examination are seen to be much increased in density, even to appear quite solid and devoid of medullary cavity, particularly the metaphyses, which may be marked off from the shaft by a less dense band and by a sudden diminution in diameter of the bones, especially the upper tibia and lower femur. There may be alternate denser and lighter bands. On running the fingers down the shaft of the femur a shelf-like alteration in the thickness of the bone towards the lower end can be detected, especially in young children. The fractures, which do not appear to be as common in this affection as in osteogenesis, are sharp and transverse, and often correspond to transverse lines of lessened density. Calcification may also be found in the dural folds and in the ligaments. Optic atrophy is frequent. Retarded growth, hydrocephalic changes, imperfect dentition and some irregular thickenings on the skull may be present. Parsons and Barling emphasize the severity of the anæmia which may be associated with it, and say the prognosis for this reason is grave in childhood. In two personal cases the hæmoglobin was reduced to 21 per cent. and 47 per cent. respectively. Contraction in size and obliteration of marrow spaces leads to myelophthistic anæmia. Leuco-erythroblastic anæmia may be identified.

An enlarged liver and spleen may be present especially in very young cases and this may be related to extra-medullary hæmatopoiesis. In a recently-observed child aged three years the general pallor was so extreme as to resemble that of leukæmia ; the spleen and liver occupied most of the abdominal space, and the blood showed reticulocytosis of 14 per cent. and erythrocytes 2·2 millions. Whether or not the disease is ever acquired in adult life seems questionable. Probably it is a developmental error beginning early in life. If free from complication it may easily be overlooked till adult life, and then perhaps only discovered by accident. The bone changes may occur without any anæmia. Fairbank observed a patient, seventy-five years of age, with this bone disorder. Mild or partial cases affecting one or several bones have been seen. One such case, showing a patchy distribution of the dense areas in the bones, was reported by Wakeley. In this case the red cell count and the hæmoglobin were rather above normal (fig. 498*a*, *b*, *c* and *d*).

Osteopathia condensans disseminata (osteopœcilie or osteopoi-

kilosis).—In 1915 Albers-Schönberg described another and entirely different affection of the skeleton, which is sometimes called by his name. This apparently causes no symptom or signs, other than those seen in X-ray photographs and has always been discovered by accident. It is not associated with fragility. The condition is characterized by the presence of innumerable dense spots in the bones. The spots are about the size of a pea and are round or oval in shape, the long axis corresponding to that of the affected bone. They are seen in the metaphyses and especially in the epiphyses of the long bones, in the carpus, tarsus, pelvis, scapulæ, vertebræ and skull. The condition is rare; it may be familial, and has been seen at all ages from fœtal life to over sixty years (Fairbank). Fairbank has described the condition associated with disseminated lenticular dermato-fibrositis.

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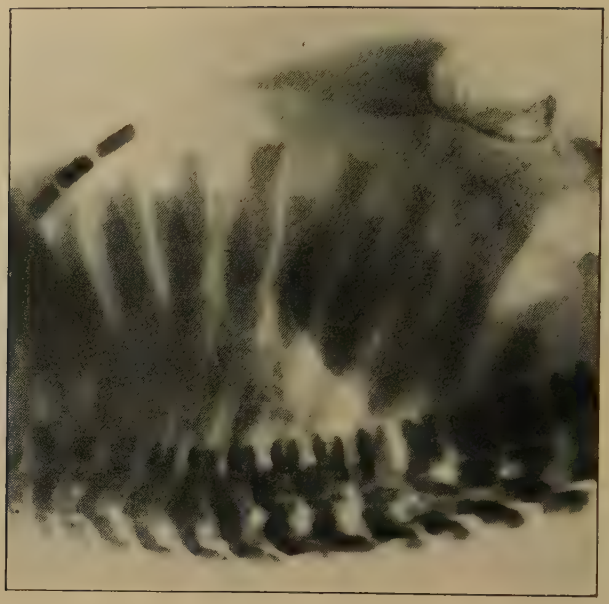
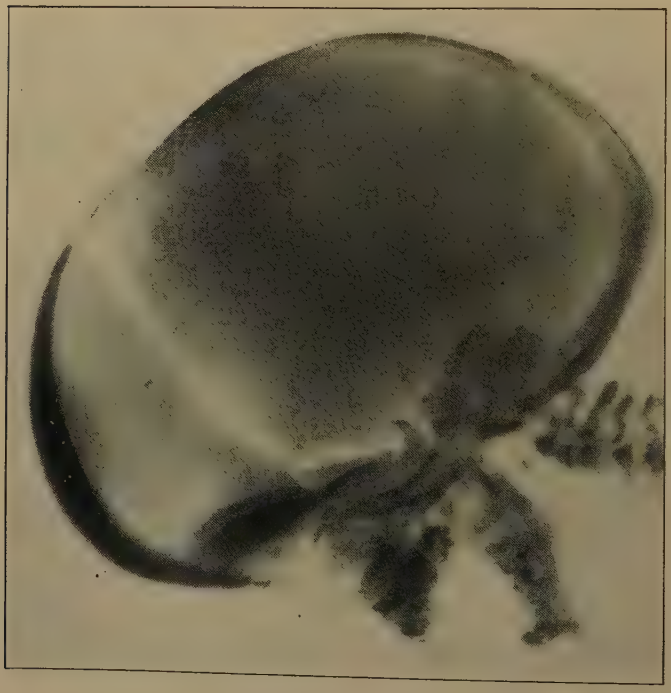
Osteitis Fibrosa Generalisata

In 1935 Hunter said, " A decade ago we had no proof of the relationship between parathyroid activity and the metabolism of phosphorus and calcium. The discovery of the parathyroid hormone placed in our hands the explanation of generalized osteitis fibrosa of von Recklinghausen; the widespread pathological resorption affecting all the bones is the effect of a parathyroid tumour." This is a rare disease in childhood.

Hunter mentions a child aged thirteen years, and Joll records a case which probably began about puberty when bending of the bones was observed and later the typical multiple cystic bones occurred. Dyke *et al.* record a girl aged fourteen years who complained of " rheumatism " and painful walking in whom a parathyroid tumour, 30 mm. in length, was removed. The same authors record a second case of a girl aged fourteen years who had progressive deformity of the bones for four years and which a parathyroid tumour weighing 5 grammes was excised. Clubbing of the fingers was present in this case. An excellent clinical example of the disease is related by Mimpriss and Butler, a boy of seventeen years (apparent age fourteen) with pains in the knees and percussion tenderness over the long bones; general skeletal osteoporosis with some cystic changes in one tibia and mandible; serum calcium 18·8 mgm., phosphorus 2·9 mgm., and blood urea 66 mgm. per cent. A parathyroid tumour, 12 mm. in length, was found and removed, after which the serum calcium fell to 10 mgm. and phosphorus rose to 4·3 mgm.; the blood urea decreased to 28 mgm. per cent. and the child made a complete recovery. The case of Pemberton, a girl of fourteen years, had bouts of vomiting and polyuria with polydipsia over a period of three years. Ultimately the cause was traced through blood chemistry studies and a parathyroid tumour 12·5 mm. in size removed, with complete recovery. Urinary symptoms (without calculus) as nocturia, enuresis and polyuria of four years' duration were associated with forearm fractures in a girl aged thirteen years, who was proven to suffer from primary hyperparathyroidism (Castleman and Mallory).



(b)



(a)

(*c*) (*d*)

Fig. 498.– Osteopetrosis (Albers–Schönberg Disease) in an Infant of Two Years.
(Case of Drs. R. Lightwood and R. Williams. By permission of *Proc. roy. Soc. Med.*)

The assumption that hyperparathyroidism always manifests itself in osteitis fibrosa cystica generalisata is incorrect. Albright in a series of seventy-four cases found that a third revealed no radiological or biopsy evidence of skeletal disease. Keating notes two others. The serum phosphatase is only increased in those cases in which bone disease is detectable. It is not clear why in some cases of hyperparathyroidism minerals should be drained from the bones whereas in others the skeleton is apparently not involved. Early diagnosis is therefore essentially dependent upon hypercalcæmia, hypophosphatæmia, hypercalcuria and hyperphosphaturia.

Symptoms and signs.—These include pain and tenderness of bones, sometimes with spontaneous fracture ; hypotonia and muscular weakness ; polydipsia and polyuria : anorexia and abdominal cramps ; sometimes renal calculi ; high serum calcium and low plasma phosphorus ; high plasma phosphatase ; increased output of calcium in the urine ; and radiographic evidence of generalized decalcification of the whole skeleton with or without deformity, cysts and tumours (Hunter). Radiographic examination of the hands is often very informative and usually reveals any changes which have occurred in the skeleton. The bone changes are due to lacunar resorption of calcified bone by osteoclasts and trabeculated cysts may result. Osteoclastic masses may simulate tumour nodules, especially in the mandible. Osteoporosis precedes the cyst-like changes. Raised blood calcium—12 to 25 mgm. per cent. and low blood phosphorus —1 to 2·5 mgm. per cent. ; and abnormal urinary excretion of calcium and a negative calcium balance are conclusive.

If a parathyroid tumour can be found and removed, brilliant cure will result and bone pains vanish rapidly, but it should be kept in mind that the quick fall in blood calcium may cause latent or manifest tetany to occur temporarily.

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Fibrous Dysplasia of Bone

Under this name Falconer and Cope (1942) discuss and illustrate a remarkable disease which has now been recognized as a definite clinical entity of childhood. It is characterized by a peculiar fibrous dysplasia of the bones with cystic changes, patchy brown pigmentation of the skin, and, in girls, precocious sexual changes (fig. 499).

Weil (1922) published the earliest case. Braid (1939), described a girl, aged nine years, whose sexual and skeletal development was equal to fifteen years; menstruation occurred since infancy; and there were several spontaneous fractures and areas of skin pigmentation. Albright (1937) brought the recent description forward. "The recognition of this disease is important, because it segregates a group of cases until recently confused with other types of bone dystrophy and specially with generalized osteitis fibrosa (von Recklinghausen) with the result that in a considerable proportion of the cases a fruitless exploration of the parathyroids has been done."

FIG. 499.—FIBROUS DYSPLASIA, AGED TEN YEARS. (Dr. Braid's Case.)

The patient may reach middle age before the disease is recognized, *e.g.* the case described by Dockerty *et al.* wherein despite widespread distribution of skeletal lesions a fracture, at the age of fifty-one years, was the first link in diagnosis; however, in this case menstruation had occurred at seven years of age, and growth was fast until the age of fourteen, when she stopped growing and had a final height of only 4 feet 11 inches.

Ætiology.—Albright suggests that a hypothetical neurological disturbance causes the bone or pigment changes and likewise initiates the endocrine effects. Falconer thinks that a congenital disorder of development involving the bony skeleton and the hypothalamus may be responsible. Braid considers that the neonatal icterus gravis with acholic

stools, and of several months duration, a striking feature in four of the recorded cases, to be of ætiological significance. She quotes experimental and clinical evidence to show that a relationship exists between liver disorder and bone dystrophy, and suggests that the responsible liver disorder in these cases is the direct result of the neonatal obstructive jaundice; also the endocrine disturbance may be the result of damage to the hypothalamic region in the central nervous system. The parathyroid glands are not enlarged.

General features.—The disease occurs about equally in both sexes and there is no evidence of heredity. Other children in the family are usually normal. A woman who had the disease in childhood did not transmit it to her children. The onset, is insidious, progresses during childhood, and the active phase seems to end at adult life. Skeletal deformity or pathological fracture may be first noted, but areas of characteristic brown skin pigmentation may lead to early detection. Bone changes have been observed as early as the first year and are always in evidence by the age of ten years. In the female irregular menstrual bleeding may be the first symptom and has been noted in the first year of life. Visual deterioration may occur from the effects of skull changes. The bony dystrophy is indicated by the presence of multiple areas of fibrous dysplasia, both membrane and cartilage bones may be involved, but there is no generalized decalcification of the skeleton. The femur is the most commonly affected bone. The dysplastic areas start in the narrow spaces of the diaphysis and gradually expand, and fairly vascular fibrous tissue may be irregularly deposited. Robb-Smith finds histological differences from the osteitis fibrosa of hyperparathyroidism. By progression the bone is thinned from within and the shaft expanded. In some cases the osseous changes are very asymmetrical and may for a time remain unilateral. This process and even fractures are usually painless. Skeletal distortion, as coxa vara, kyphoscoliosis, and genu valgum occur. X-ray examination reveals a loss of normal bone pattern, and the appearance of irregular trabeculation and pseudocystic zones. The face may show gross asymmetery, the eyeball of the affected side tends to proptosis and some displacement downwards and outwards. Some cases of leontiasis ossea may really belong to this group. Cranial nerve pressure, especially the optic nerve, may occur as a result of the sclerotic process in the skull. Deafness and anosmia may also occur. The skull may reach over one inch in thickness and appear to resemble that seen in Paget's osteitis deformans. The cephalic veins are prominent. In comparison with hyperparathyroidism the serum calcium and inorganic phosphate are usually normal and calcium balance normal. Phosphatase rises and in one of Braid's cases has gradually reached 200 units. Skeletal precocity is frequent and is indicated by generalized early development of epiphyses, and rapid growth of the skeleton, thus the child may be big for its age. Epiphyseal union also is accelerated so that the adult patient may be small. This skeletal precocity may occur apart from sexual precocity, but doubtless it is of endocrine origin.

In the female cases sexual precocity is a prominent feature; menstruation and essentially feminine secondary sexual characteristics may appear and lead up to regular menstrual cycles at the early age of three years. The ovaries, adrenals, and the urinary gonadotropic and œstrogenic hormone are usually normal. Rarely some degree of sexual precocity may appear in the male. Gynæcomastia may occur. Intellectual levels are normal. The thyroid gland is nodular or diffusely enlarged in some cases and occasionally a high B.M.R. is found; and a suggestion of acromegalic dyspituitarism is sometimes apparent. The cutaneous pigmentation is shown by areas of medium brown skin of normal texture. It may affect any region. In personally observed cases it has been present on the face, neck and chest. More commonly it is seen on the lumbar and thigh areas; there is no correlation between the presence or extent of pigmentation and the bone changes. Lichtenstein has described the same bony dystrophy, under the term of polyostotic fibrous dysplasia, and Albright has reviewed its place among apparently related diseases.

Prognosis.—The disease becomes stationary in adult life. It is not fatal. Fractures heal well. Mentality remains normal. Reproductive functions are usually unimpaired.

Treatment.—In view of the lack of definite ætiology, symptomatic treatment of impending or actual deformity and fracture is all that can be offered at present.

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Melorheostosis

In 1922 Léri described a condition of irregular deposits of bone running along the bone periphery and resembling candle dripping, to which he gave the term "melorheostoses." It is sometimes referred to as the Léri type of marble bones. It is a rare condition in which portions of certain bones are petrosed. The outline of the affected bone is definitely distorted and there is pain, usually of the dull aching type and occasionally severe with some limitation of movement in the joints formed by the affected bones. The onset probably occurs in childhood but the symptoms may be delayed. It affects both sexes but is not hereditary or familial. The affected limb may be altered in its length. There is no undue fragility. X-ray examination shows parts of certain bones to be dense and thickened and this may affect one side of a long bone. In the forearm or leg one bone only may be affected. The scapula or pelvis may show dense patches. Distortion of outline and cortical thickening is a more common feature in the arm. The increased density may extend to the soft tissues near a joint. Deformity such as curving of a bone, genu valgum or distortion of the fingers may be present.

FIG. 500.—MELORHEOSTOSIS.

Photograph of patient to show: (1) Deformity of affected fingers; (2) Facial adenoma sebaceum; (3) Macrocephaly due to severe internal hydrocephalus.

FIG. 501.—X-RAY PHOTOGRAPH OF AFFECTED HAND.

(By kind permission of Dr. G. S. Hall and the *Quart. J. Med.*)

Hall (1943) has given an account of the changes as seen in tuberose sclerosis. He regards it as a local disorder of osteogenesis characterized by periosteal deficiency, especially in diaphyseal bone, and a spread of ossification from affected bone to adjacent tissues even to involve subcutaneous tissue and skin. The areas of affected bone show localized increased density. It may be painful and cause some limitation of movements of joints. Hall's photographs show the nodular enlargement of finger bones, deformity of the affected fingers, facial adenoma sebaceum, and macrocephaly due to internal hydrocephalus –all manifestations, he believes, of inherent mesodermal effect (fig. 500 and 501).

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CHONDRODYSPLASIA

Chondro-Osteo-Dystrophy

It is generally accepted that Brailsford (1929) and Morquio (1929) divide the honours in the earliest adequate descriptions of this type of chondrodysplasia. Brailsford laid particular stress on the radiological, and Morquio on the clinical features. It has therefore been referred to as the Brailsford-Morquio dystrophy. Many degrees of the condition exist, some so slight as to escape clinical detection, others resulting in variable degrees of deformity. It may even be initiated *in utero* and be detected in the skeletons of still-born babies. Severe degrees of the dystrophy may develop in later years of childhood when earlier skeletal X-ray pictures are apparently normal. Hereditary factors are definite and the disease may be present in several members of a family. Morquio described four in a family of five. Ruggles (1931) records the condition in the first, fourth and seventh children in a family of seven. Both twins have been affected (Neale, 1934). The dystrophy affects skeletal bones but leaves those of the skull unaffected. The prominent deformities are those of the spine and chest so that the child's appearance suggests the existence of a cervical caries, with the head sunk into the chest. The vertebral bodies are shallow and relatively broad. In the limbs there is absence or retarded growth of the epiphyses, and a widespread defect of calcification. At birth the children are apparently normal, and the first clinical evidence of the affection usually appears when they begin to walk, the gait being awkward and waddling owing to the epiphyseal lesions, especially at the hip-joint. The deformities progress rapidly for some time and then cease to increase but leave a characteristic deformity of the skeleton (fig. 502 and 503).

Symptoms and signs.—There are cases with slight but typical X-ray changes with lack of any mentionable external deformity although some

FIG. 502.—CHONDRO-OSTEO-DYSTROPHY (BRAILSFORD-MORQUIO SYNDROME) IN TWINS.

FIG. 503.—CHONDRO-OSTEO-DYSTROPHY.

restriction of joint movement may be stated. Brailsford's original case, shown at Royal Society of Medicine in 1928, is worth noting.

"A boy aged $3\frac{3}{4}$ years appeared normal until he was five months, at which time the mother detected a small kyphos in the dorso-lumbar region. He began to walk at thirteen months. It was then noticed that the boy could not stand erect, but stood and walked with the body supported by the hands on the knees. The child was bright and intelligent and looked relatively well-nourished. At the age of ten years he was $2\frac{3}{4}$ feet in height and could stand almost erect without supports and walked with a normal gait, but readily tired. His joints were all enlarged, but there was no evidence of wasting. The neck was short and thick. He grew only 2 inches further between 10 and $13\frac{1}{4}$ years of age, and declined in physique and walking; the musculature became flaccid and atrophied."

Morquio wrote:

"The whole body presents a marked deformity characterized by a longitudinal shortening and an anteroposterior deepening of the thorax with the sternum projecting into a point, the whole thing forming a contrast with the extremities, which though deformed have normal dimensions giving the whole appearance of children with Pott's disease with an extensive gibbus. The genu valgum, the flat foot, the malformation of the vertebral column, the weakness of the muscles and the tendons give rise to a difficult gait, resembling that of a duck."

In the cases observed by the writer a cheerful disposition, a bright intelligence and a ready smile has formed a strong contrast with the definite physical disability.

This dystrophy attracts attention in X-ray examinations because of the irregular growth of the epiphyses, primary and secondary ossific centres being involved. Stippling and fragmentation of epiphyses occurs.

Irregularity of primary ossifications may be most striking in the vertebral bodies, especially in the dorso-lumbar and cervico-dorsal areas where defective development of the articular processes may lead to displacement and kyphotic deformity (fig. 504).

Brailsford describes four groups of changes. (*a*) Large joint spaces; irregularity and multiplicity of the osseous nuclei for all the epiphyses; irregular shape and size of the vertebral bodies and dislocation in the lumbo-dorsal region; the long bones are shortened and thickened with coarse irregular cancellous tissue and absence of the regular line of the lamellæ. (*b*) In this group the active phase appears to cease before puberty. The disorganization of the metaphyses causes shortening of the limb bones and pressure deformity of the ends of the long bones and of vertebral bodies. (*c*) Herein the changes are chiefly confined to the spine or hip-joints and less frequently the knees. There may be no ossification of the femoral head or neck on either side, and the acetabula are irregular in outline. (*d*) The only change detectable may be confined to the vertebræ, the bodies being irregular, wedge shaped and reduced in size. The anterior half of the first lumbar body may be absent, and so this vertebra is displaced backwards producing angulation at this level.

In summary therefore the dystrophy may affect the spine only, the spine and proximal joints, or the whole skeleton. Resultant deformity depends on the severity of the lesions and the subjected pressure. Brailsford (1943) has described an unusual osseous dystrophy characterized by dense epiphyses which fuse early, although development of other ossific centres is markedly delayed; in this case grotesque dwarfing with apparently normal intelligence was associated with severe spinal curvature and bilateral coxa vara. It is a matter of considerable clinical interest to compare chondro-osteo-dystrophy (typical and atypical) with the "gargoylism" group. Romanus (1940) has added to the descriptive radiology and Fairbank (1951) notes similar changes in the spine in some cases of cretinism.

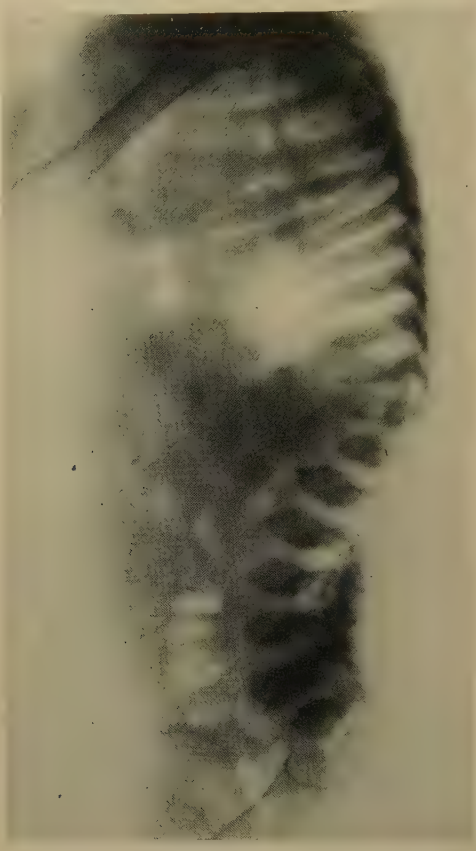

Fig. 504.—Osteo-Chondro-Dystrophy.

Prognosis.—Dwarfism remains in the severe types. An adult case can be recognized by the shortened neck, the kyphosed occiput due to moulding of the skull base over the upper cervical spine and growth disturbance in the cervico-dorsal vertebræ. Kyphosis persists and marked lumbar lordosis is a late feature. Ellman has noted a possible confusion with the late arthritic manifestations of rheumatoid disease.

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Chondrodysplasia

Synonym.—Dyschondroplasia.

The beginning of the recorded type of bone disorder now grouped under this name dates from 1899 when Ollier of Lyons described under the term of dyschondroplasia a disturbance of the growing parts of the skeleton, with nodosities and swellings of the corresponding long bones, diaphysial curvature and hand deformity, and emphasized the clinical asymmetrical or unilateral involvement of the body. This wa before X-rays were used in the systematic study of the skeleton and in the light

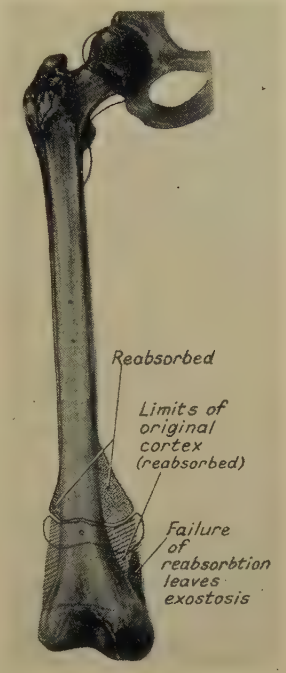

Fig. 505.—Diagrammatic Representation of Growth of Femur.

The two dots in the centre of the bone do not change relationship with growth, but the circles in the epiphysis move away from the dots in the central portion. The dotted and shaded areas indicate the limits through which the bone develops in the adolescent to adult period. It is in this area of rapid growth that most changes occur in dyschondroplasia. Reabsorption normally results in diaphysis becoming more narrow than the metaphysis. Partial failure of the process (diaphysation) results in exostoses ; complete failure results in broad metaphyses.

(By kind permission of Dr. J. R. J. Mahorner and the *J. Pædiat.*, 1937.)

of further observation the unilaterality has been shown to be much less in evidence. Ollier recognized the fundamental lesion as a disturbance in the growth of the epiphyseal cartilage and ossification of the metaphyses. Since then numerous varieties of the disorder have been recorded under such names as hereditary multiple exostoses, diaphyseal aclasia, hereditary deforming chondrodysplasia, familiar chondrodystrophy, multiple congenital osteochondromas and multiple cartilaginous enchondromas. Ehrenfried (1917) observed the prevalence of cases of multiple exostoses, and emphasized the hereditary basis and demonstrated a true dysplasia of cartilage cells in the epiphyses. Fairbank draws a sharp distinction between exostoses and dyschondroplasia, emphasizing in contrast, that exostoses are frequently hereditary, occur in almost any bone and affect the surface.

In the ætiology congenital and familiar factors are clearly established, with some preponderence in males. Multiple exostoses may pervade every generation of an affected family and is the most dominant and potently transmitted type. The cause of the disordered bone growth is unknown (fig. 505).

Exactly what takes place at the epiphyseal line in chondrodysplasia is obscure, but the growth of cartilage appears excessive and calcification irregular. Collections of cartilage cells separated by bony partitions parallel or irregularly arranged, are found in the metaphysis and nearby diaphysis.

Multiple exostoses or diaphyseal aclasia.—The outstanding features are the formation of exostoses near the extremities of the long bones, and failure of adequate bone modelling in the same zones. Even in the infant small bony buds may occur from the sides of the diaphyseal extremities and these small buds grow until the epiphyses have fused. Some remain small, others enlarge very considerably. Coarse cancellous trabeculæ develop therein. They may grow also from the pelvis or vertebræ; spinal cord compression may so occur. Apart from the exostoses bone growth may be checked and so induce some deformity due to unequal length of long bones, possibly also causing partial dislocation at a joint. Sarcomatous changes have been noted rarely. Rapid increase in size of a tumour, especially after the epiphyses have fused, should rouse suspicion.

Ætiology.—Males are more often affected than females, in the proportion of two to one. This condition is hereditary, may be familial and be transmitted by males or by females. Unaffected females may transmit the affection, and hence it may appear that males more often transmit it. An affected individual who marries a normal person transmits the condition to about half his offspring (Gossage and Carling).

Morbid anatomy.—The exostoses, while growing, are tipped by a layer of hyaline cartilage. The surface may be covered by a bursa. They arise from bones formed in cartilage, and especially from the diaphyses of the long bones—such as the femur, tibia, humerus, radius and fibula, near the epiphyseal plate. As the bones increase in length the distance between the epiphyseal plate and the exostosis increases. They are most frequent around the knee, at the upper end of the humerus and the lower end of the radius, thus corresponding with the favourite sites of osteoclastoma. They vary much in size and shape, but tend to rise abruptly from the surface of the shaft towards the centre of the affected bone, while they slope away in the direction of the epiphysis.

Pathogeny.—The condition appears to depend on an inherent vice of development. Keith, adopting the term diaphyseal aclasis, regards the condition as a disorder of growth confined to the bones at the junction of membranous and cartilaginous formation, and not as a tumour; he places it in the same category as achondroplasia. Weber suggests the title periosteo-dysplasia, and draws attention to the occurrence of

agenesis of the distal end of the ulna causing shortness of the forearms; this may also occur without multiple exostoses. Lardennois and Nathan regard the immediate cause as absence of the periosteal bone which allows a hernia of endosteal bone. The blood calcium is normal.

Clinical picture.—The patient is normal mentally, and usually has good muscular development, and may even be inclined to athletic activities. The tumours may be few or extremely numerous—even up to 1,000 (Chiari). Though they have been noted at birth, they usually appear in childhood and increase in number and size up to the time when epiphyses unite at about the twenty-fifth year, when they usually cease to grow, and even appear to get smaller, but they may continue to grow until late in life. They are usually painless, but during their growth they may cause some discomfort and tenderness; occasionally a tendon may slip over a prominent bony outgrowth. Deformity is not an important feature, but may be observed in older children; this is variable but some forms are more characteristic, *e.g.* varus at elbow; dislocation of the radial head; ulnar deviation of the hand; valgus at the knees or ankles. Gait and stance may be abnormal. Short stature is common. Unilateral emphasis will reveal shorter extremities on one side. Facial asymmetry may also be evident. Sarcoma may arise in cases of multiple exostoses. Platt records a large and rapidly growing chondroma arising from the cap of an exostosis in a case of diaphyseal aclasis.

Diagnosis.—As exostoses may occur in myositis ossificans progressiva, the presence of bony growths in the muscles must be looked for. Restriction of movement, which is such a prominent feature in myositis ossificans, is absent or limited to a single joint in multiple exostoses. X-ray examination shows the exostosis as a hook-like process which invariably points away from the epiphyseal plate. Multiple enchondromata are found in the phalanges of the hands and feet, and grow from the inside of the bone which they expand. Treatment is unnecessary unless inconvenience results from the size of an exostosis, or when important nerves or blood vessels are affected. If operation is demanded for one, other exostoses likely to cause trouble in the future should be removed at the same time. Removal must be complete or growth will continue.

Multiple chondromata.—Hereditary factors are usually absent in multiple chondromata which radiographically appear as defects or gaps in the ossification of the bones. Though asymmetrical the lesions are generally bilateral. Limb deformity may occur due to disturbance in bone growth. Metaplasia into sarcoma may occur. Multiple chondromata spring from the centre of the phalanges and bones of the carpus and tarsus, tumours of the fingers being specially prominent. The condition may be familial and is an inborn disorder of growth of the long bones and belongs to the same group as multiple exostoses. In some cases the lower ends of the radius and ulna may show cartilaginous tumours. In Ollier's disease the tumours are almost unilateral in their distribution and are associated with diminution in length of the affected

arm and leg. The tumours, which usually cease to grow about the time that the epiphyses unite, expand and thin the bone, are prone to degenerate, and from myxomatous change may become cystic. A natural tendency to calcification may occur. They may fluctuate or give egg-shell crackling, and the skin over them is stretched and shows dilated veins, in severe cases. Considerable deformity results, and the hands may be useless. They must be distinguished from tuberculous dactylitis, in which suppuration is prone to occur, and from syphilitic dactylitis by the presence of concomitant disease. Boggs reported a case associated with degeneration of the cranial nerves and muscular dystrophy.

In view of the fact that the chondromatous lesion may considerably destroy the bone and so impair its physical power it is sometimes considered advisable to excise the abnormal tissue in order to save a neighbouring joint surface or avoid a pathological fracture. Orthopædic surgeons have devised conservative operative measures for this purpose. The tumours in the fingers usually prove to be the real trouble, and the possible hideous deformity which may arise is well shown in a case recorded by Rae. Operative treatment is, however, usually confined to the hands. Irregular growth at the epiphyseal lines, causing deformity, for instance—genu valgum—may call for operative correction, the operation aiming at the deformity not the cartilaginous tumours.

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Tarso-epiphyseal aclasis.—This condition was first described by Monchet and Belot (1926) under the title " tarsomégalie " and is extensively studied and illustrated by Trevor (1950). There is a congenital growth disorder of the tarsus and of the epiphyses of the lower limbs and the disorder was found in seven boys and one girl, and between the ages of nine months and ten years. The left lower limb was affected five times and the right three times. Deformity and limited movement of knee or ankle joint may be the presenting sign and X-ray shows characteristic epiphyseal changes with nodular swellings distinguishable from chondrodysplasia and diaphyseal aclasis wherein the essential changes are in the metaphyses. Degrees of irregular and asymmetrical epiphyseal growth

is seen and the bony outgrowths may be variably stippled. The cause appears to lie in a failure to confine the peripheral cartilaginous cells, derived from the mitotic annulus, within the normal sphere of epiphyseal development. Surgical reconstruction of the abnormality has been successful.

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Maffucci's Syndrome

The first recognizable case of chondrodysplasia with hæmangeiomata was described by Maffucci in 1881. Kast also recorded the clinical picture in 1889. Recently Carleton *et al.* (1942) re-emphasized the condition in which the association of one or more forms of chondrodysplasia is linked with the vascular hæmatomata (cavernous angeiomata and phlebectasia). It is suggested that the two components of the syndrome have only a coincidental association and belong to the group of congenital mesodermal dysplasias (fig. 506).

Bearing in mind the general subject of mixed syndromes in chondrodysplasia Ellis (1940) observes the possible association with ecto-dermal dysplasia affecting hair, nails and teeth, and polydactly and congenital morbus cordis. The condition was held to be due to a Mendelian recessive factor, without sex-linkage.

FIG. 506.—MAFFUCCI'S SYNDROME.

Boy aged eight years. Right leg smaller than left; multiple angeiomata.

(By kind permission of Dr. Carleton *et al.* and the *Quart. J. Med.*)

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Infantile Cortical Hyperostosis

Under the title "infantile cortical hyperostoses" Caffey described a new syndrome in infants in which there were recognized tender swellings in the soft tissues, and bone thickenings in the skeleton due to cortical hyperplasia under a proliferating periosteum. The usual age of onset is under three months and initial signs have appeared at the age of three weeks. Fever, increased sedimentation rate, raised serum phosphatase, anæmia, leucocytosis and some pyrexia are usually found. Trauma would appear to play no part and no known infecting agent has been detected. The pathogenesis is obscure. The soft tissue swellings may be located in the scalp, face, neck, thorax or limbs. Among the bones affected by

hyperostosis the mandible and the clavicles are involved most frequently, but the changes have been revealed radiologically in the calvarium, ribs, scapulæ, long bones and the metatarsals.

The tender soft tissue swellings may be associated with " pseudo paralysis ". The lower jaw may be swollen or the clavicles thickened. The layered osteoblastic periosteal reaction may be followed over a period of months, the natural history passing through remarkable bone thickening to a final clearing and healing (Sakula). In the 28 cases reviewed by MacGregor and Davies swelling in the face or in a limb was an early sign and soft tissue swellings were most commonly detectable in the face, forearm and legs. O'Reilly noted that the serum calcium and phosphorus remain within normal limits although the serum phosphatase in his case was high. The clinical signs might suggest periostitis, but syphilis is excluded in the history and negative serological evidence. In the healed phase the bones may appear larger than their chronological age.

During the active stages of the disease, general resistance is lowered and there is some danger from secondary infection (Matheson and Markham). Pleural effusion with monocyte reaction has been detected in some cases. X-ray examination will usually disclose multiple cortical hyperostoses, but there is no evidence of hæmorrhage or inflammatory cellular infiltration on biopsy.

The treatment of this disorder is essentially general nursing and maintenance of nutrition. Excessive irritability, variable anorexia and slow weight gain may involve special nursing difficulties (Burke). Antibiotics are ineffective except insofar as associated respiratory infection may deem their use necessary. The associated anæmia may need remedial blood transfusion. Natural resolution of all the lesions is usual but a period of several months to two years may elapse before all the signs disappear clinically and radiologically (Fairbank).

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Progressive Diaphyseal Dysplasia

(Engelmann's disease)

This is a rare type of bone dystrophy first described by Engelmann in 1929 under the name " osteopathia hyperostotica (sclerositans) multiplex infantilis " and has been most frequently recognized between four to

ten years of age, but Gillespie and Mussey describe the disorder in a girl aged two years. The symptoms are not obvious but may include difficulty in walking, with a peculiar waddling gait, some limb pains and even bone tenderness with possibly palpable thickening of long bones. Some cases may show underdevelopment of the musculature. Engelmann noted splenomegaly in his original case. Poor general nutrition and an abnormal fatiguability has been observed. Minor variations in the tendon reflexes may be detectable. The cause is unknown and it may be a congenital developmental error. There is no known familial or hereditary incidence and there is a male predominance in incidence. There are no significant biochemical or cellular changes in the blood. Biopsy reveals exceptionally hard bone containing broad, dense, bony trabeculæ with histological sclerosis and some fibrosis in the adjacent marrow (Lavine and Koven).

X-ray changes in the long bones is confined to the diaphyses, the metaphyses and the epiphyses being uninvolved. The essential appearances are a progressive symmetrical fusiform enlargement and cortical thickening in the diaphyses which suggest that the main lesions are a progressive endosteal and periosteal new-bone formation with some narrowing of the medullary canal. Gradual extension of the bone changes and involvement of further bones may be observed over a period of years. The basal and frontal parts of the skull may show variable thickening.

In the differential diagnosis osteopetrosis, polyostotic fibrous dysplasia, hypervitaminous A and infantile cortical hyperostosis have to be considered and it is significant that fever and leucocytosis are absent. The sedimentation rate and alkaline phosphatase are normal. This type of bone disease has been described over the age of twenty years (Stronge and McDowell) and it would appear to have a prolonged natural history.

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Myelosclerosis

In myelosclerosis the essential change is an obliteration of the marrow cavity by fibrous or bony tissue which may proceed to osteosclerosis. The change has been recorded in erythroblastosis fœtalis by Follis. Hickling notes that the frequency of osteosclerosis in myelosis (leukæmic or non-leukæmic) is not known. Myelosclerosis may occur in childhood and has been found in association with leukæmoid and leuco-erythroblastic blood states. Splenic enlargement is present and the general picture may suggest splenic anæmia. X-ray of the bones shows characteristic increased generalized density and marrow obliteration; and attempts at marrow puncture may be difficult. Variable or continued fever and anæmia may be prominent. It must be kept in mind that the splenic

enlargement may be related to an attempt to mobilize extramedullary hæmopoiesis and splenectomy may be strongly contra-indicated.

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TUBERCULOUS DISEASE OF BONES AND JOINTS

As tuberculosis specially attacks the cancellous tissue of bone, and thence readily spreads to the adjacent joints, and, further, since tuberculous disease of joints is often secondary to disease of the adjacent bones, the two conditions are closely related, and will be considered together.

Although tuberculosis in bones and joints usually appears to be primary during life, it is really secondary to some focus, often of small size, the bacilli being conveyed by the blood-stream. Injury, by reducing the local resistance of a bone, favours the growth of tubercle bacilli. According to most of the available evidence the bacilli of bone disease are of the human and not of the bovine form, but out of seventy cases of tuberculosis of bones (31) and of joints (39) of children in Edinburgh, 41, or 58 per cent., were due to the bovine form, 26 to the human form, and three to both forms (Fraser). Tuberculosis of bone is rare in the first three months of life. The favourite sites of tuberculosis of bone are the vertebræ, the ends of the long bones, the tarsus, carpus, ribs, and sometimes the skull. It has been estimated that a third of the cases in children occur in the spine, another third in the hip, and then with decreasing frequency in the knee, ankle, elbow, shoulder. The favourite site for a tuberculous deposit in bone is the cancellous tissue at the end of the shaft of a long bone, the so-called juxta-epiphyseal region, and it is of considerable importance that the inflammatory disease may travel through the epiphyseal cartilage and so involve the epiphysis and the joint. An important feature in the X-ray appearances of these cases is the almost invariable absence of new bone formation under the periosteum, a condition rarely met with when pyogenic organisms, *e.g.* staphylococci, are the cause. It must be stated, however, that some variation in the radiological appearances is not unusual ; rarefaction of the adjacent bones is usual but sometimes unexpected denseness is seen.

Tuberculous dactylitis.—The metacarpals and phalanges are enlarged, spindle-shaped, and tender from the presence of caseous material in the interior of the bones. The lesions are multiple. The shafts of the bones become thinned and expanded (spina ventosa), and the caseous material may soften into an abscess and perforate, thus setting up periostitis and even a subcutaneous collection which may burst through the skin. There is a formation of new subperiosteal bone in dactylitis, and in this particular, dactylitis differs from tuberculous disease of bones in general. The appearances must be distinguished from those of syphilitic dactylitis and of multiple enchondroma and sarcoidosis.

Tuberculous osteo-periostitis of the frontal, parietal and occipital bones may occur. Reber has collected 158 cases. It may occupy the centres of ossification, and so imitate syphilis, especially in the absence of bony lesions elsewhere. There may be numerous soft nodes on the cranial bones; as many as 29 have been recorded (Ménard and Bufnoir). Tuberculous nodes on the skull may co-exist with lesions of the long bones, caseous tubercles in the viscera, and widespread tuberculosis. The prognosis is particularly bad when the skull bones are affected by tuberculosis, and early radical operative treatment is indicated.

Tuberculous spondylitis.—Synonyms.—Spinal caries, Pott's disease. Tuberculous disease of the vertebræ attacks the cancellous tissue of the bodies and destroys the bone, with the production of caseous material. It is most frequent in the lower dorsal and rarest in the cervical regions. As the arches and spines commonly remain, even when the bodies of several vertebræ have been destroyed, the onset of kyphosis is gradual; pressure on the spinal cord may occur and is due to the pressure of an abscess, and the surrounding inflammatory tissue.

Fig. 507. — Tuberculous Spine.

The *symptoms* vary considerably according to the position of the lesion, and may be misinterpreted; thus, there may be persistent or recurrent abdominal pain imitating colic; or pain in the limbs, paraplegia, or nervous symptoms, which in the absence of any spinal deformity may give rise to difficulty in diagnosis. A retro-pharyngeal, lumbar or psoas abscess may result. Muscular rigidity of the back is a constant and valuable sign. Local pain in the spine is caused by jarring the head or the spine, as in jumping, and tenderness may be present over the spinous processes of the affected vertebræ. In many cases pain is entirely absent, the deformity being the first sign. Rigidity or local tenderness of the affected portion of the spine is a valuable sign, especially before the development of an angular curve (fig. 507).

In children the *prognosis* of spinal caries is fairly good, much better than in older subjects, provided that treatment is undertaken early.

Diagnosis.—The kyphosis of rickets, myopathies, amyotonia congenita, and chondro-osteo-dysplasia is painless, forms a wide curve instead of an acute angle, and disappears when traction is made on the legs, except in severe and long-standing cases.

Tuberculosis of the long bones of the limbs may occur in the epiphyses, but usually begins in the juxta-epiphyseal region of the shafts. Not uncommonly it extends through the epiphyseal plate into the epiphysis. It may extend to the joint either directly or via the epiphysis. The

position of the epiphyseal line in relation to the joint cavity is of supreme importance in this connection. X-ray pictures should always be taken, since a point of importance in distinguishing tuberculosis from pyogenic infection at the extremity of a long bone is the complete absence of new bone formation under the periosteum in the former, though it is almost invariably present in the latter. The disease may extend to the surface of the shaft, and form a subperiosteal abscess which either bursts into the joint or into the extra-articular tissues, according to the particular region affected. Pain and tenderness in such extra-articular tuberculosis are localized, and if the adjacent joint is still unaffected there are no signs of arthritis. It is important to remember that there may be a pre-arthritic stage of hip disease, in which either the sub-acetabular bone or the neck of the femur is the seat of the focus of infection. A painful limp results. Early diagnosis and efficient treatment may check the disease before the joint becomes infected.

FIG. 508. — TUBERCULOUS HIP.

Tuberculous arthritis is usually secondary to, and the main clinical manifestation of, tuberculous disease of the neighbouring bones. In the knee, however, Stiles found that the disease began much more frequently in the synovial membrane than in the bone.

MORBID ANATOMY.—The synovial membrane containing miliary tubercles becomes swollen, reddened, and covered with flakes of fibrin; it ulcerates and adheres to the cartilages which are eroded, and eventually the bone is exposed. If the disease is not checked the joint becomes distended with fluid, sero-fibrinous, fibrino-purulent, or purulent. In neglected cases peri-articular abscesses form. Tubercle bacilli are difficult to find in the effusion, but inoculation into animals proves their presence.

CLINICAL PICTURE.—The onset is usually gradual, though it may be quite acute, and the course is chronic. One or more joints may be affected, but the disease is seldom symmetrical. Rigidity with limitation of movement in all directions is an early and important sign. The joint becomes flexed and swollen (fig. 508), the outline of the synovial membrane is obvious, and thickening may be detected. There may be local heat, but the skin is not reddened in the early stages. Pain is a symptom of little value, as it may be absent or slight; on the other hand it may be severe, especially in the hip, in which pain is often referred through the obturator nerve to the inner side of the knee; jerking pains at night may occur, and limping is an early symptom. Muscular wasting accompanies all forms. Suppuration may occur in or about the joint. On X-ray examination the joint appears fluffy and the picture is characteristically blurred (Shenton).

Although it may be said that tuberculosis of the bone can exist before it is possible to detect bony changes in the X-ray pictures, it is equally true that a tuberculous lesion will sooner or later produce changes which can be detected. General atrophy of the bones forming the joint may be an important and apparently early sign. It should be appreciated that a negative X-ray picture in the early stages of the disease is not conclusive ; further X-ray examination should be made at intervals of a month or so. Bone irregularity will appear. Repeated negative X-rays over a period of three months will usually exclude a tuberculous lesion of the bone. Osteoporosis of the part rather than erosion may, however, be the only indication for a year or more.

Prognosis is better in children than in adults, provided suitable treatment is adopted early. Dissemination is not so likely to occur as in adults, but death may result from tuberculous meningitis. Mixed infections, as in discharging abscesses, add greatly to the gravity of the prognosis.

Diagnosis.—In the early stages acute rheumatism must be differentiated by the effect of salicylate treatment. Rheumatism of the hip may simulate tuberculous disease, but it should be remembered that cases of tuberculous disease, if neglected on the ground that they are rheumatic, suffer irreparable damage. Cases with an acute or sub-acute onset may simulate pneumococcal, gonococcal or other forms of infective arthritis, and to arrive at a diagnosis it may be necessary to aspirate the joint and examine the fluid bacteriologically. The use of tuberculin tests is open to the fallacy that there may be tuberculosis elsewhere. A negative result is more helpful than a positive. Help may be obtained from radiography. In primary synovial disease general atrophy is marked, while secondary bone disease may be seen. In primary bone disease the rarefied areas in the end of the shaft and the epiphysis are obvious and diagnostic. Tuberculous arthritis of the knee must also be distinguished from bilateral effusion into the knee-joints in delayed congenital syphilis. In cases of uncertainty in which low-grade non-tuberculous infection has to be distinguished from tuberculosis, it may be possible to excise a small portion of synovial membrane and submit this to microscopic examination or inject an emulsion into a guinea-pig. The sedimentation rate is not a specific one and therefore not diagnostic of tubercle, but it is of great value in determining the activity of the disease and the lessening of this under treatment.

Treatment.—Tuberculous arthritis should be regarded as a local manifestation of an infection which has invaded the system. Although tuberculosis of bones and joints is commonly regarded as a surgical disease, the treatment should be mainly medical. The first essential is absolute rest to the part, which should be immobilized by a suitable and simple splint without traction except in so far as this may be required to correct deformity. Continued extension may be required for a long period, especially in knee and hip disease. The patient's resistance should be increased by all available means ; children should be treated in the open air at the seaside or in the country, and should not be kept in towns.

Good food, with plenty of meat, cream, and fats should be given. Streptomycin with para-aminosalicylic acid is proving of value. In cases with secondary infection, other antibiotics are used in addition.

Operative interference should be avoided as far as possible, in order to exclude pyogenic infection. If necessary, joints may be aspirated rather than opened.

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THE FEMORAL HEAD AND NECK IN CHILDHOOD

This is a vulnerable structure especially in infancy and childhood. A wide variety of affections can be identified clinically and radiologically including rickets, chondrodysplasia, sepsis, osteochondritis, fibrocystic

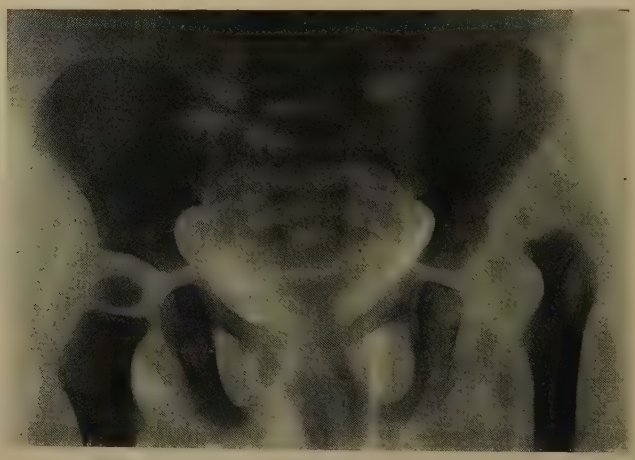

Fig. 509.—Congenital Dislocation of the Hip.

disease, congenital dislocation, coxa vara, loosened epiphysis, and protrusio acetabuli.

Congenital dislocation.—This is important because success in treatment depends very much on its early recognition. It is more common in females. Unilateral cases are about twice as common as the bilateral

ones. It may remain unrecognized until the child begins to walk, but physical signs are often detectable in early infancy; in this respect emphasis may be made on (*a*) asymmetrical natal folds, (*b*) widening of the perineum, and (*c*) telescoping of the femur. The dislocation may be complete or there may be only a subluxation. Slight displacement might possibly be overlooked when only a little of the upper end of the femur is ossified. In unilateral cases a limp, and in bilateral cases a waddling gait, without pain and without appreciable restriction of general activity, is observed. The affected limb is shortened ($\frac{1}{2}$ to 2 inches) and the pelvis drops on the other side. Lordosis is seen in the bilateral disease. The great trochanter is more prominent and the displaced femoral head may be palpable. Separation of the upper part of the thighs and of the perineum results and the groin creases are asymmetrical. It has been known for many years that a poor acetabulum is the outstanding feature of the congenital malformation.

Radiographically the acetabular cavity is shallow, and ossification of the femoral head is delayed (fig. 509). Fripp described a case of congenital dislocation of the hip on one side and osteochondritis on the other side.

Coxa Vara

The angle between the neck and shaft of the femur is reduced from the normal childhood 160 degrees to a right angle or less. Weight bearing, acting mechanically upon a femoral neck weakened from any cause, will produce the effect. In children, the causes may be divided into three main groups; (1) infantile coxa vara; (2) in patients with bone disease causing softening of the femoral neck; (3) as a result of slipping of the femoral epiphysis.

In the *infantile* or *congenital* form of coxa vara the femoral neck shows an abnormal ossification. It is often bilateral but may be quite asymmetrical. The lordosis, rolling gait, raising of the trochanters, loss of abduction, small stature and absence of pain are conspicuous features. The average age of recognition is about six years; in Ollerenshaw's series of sixteen cases the youngest was two years and the eldest eleven years. Radiography shows a clear area in the neck of the femur distal to the epiphyseal line, a shortened neck and decreased angle, and sometimes a translucency of the femoral head and some shelving of the upper part of the acetabulum (fig. 510). The cause is uncertain; Fairbank shares the view of most surgeons in regarding this type as a developmental error and notes that quite often the radiographic appearance on the two sides is remarkably similar, each showing a separate triangular fragment. Ollerenshaw notes the absence of trauma and favours "aseptic necrosis." Brailsford considers it to be a localized dysostosis. If untreated the femoral head eventually comes to lie several inches below its normal position with almost no neck at all. Thus there is complete inability to abduct and a very difficult gait.

Slipped epiphysis occurs in children from about ten to fifteen years of age. Trauma alone is apparently not the cause. However the view is

held that there is an antecedent condition favouring displacement, though this may not be apparent in X-ray pictures, and that trauma, which probably would not damage a normal joint, either starts the slipping or displaces the head. Teall suggests an osteochondritis at the epiphyseal cartilage. Ollerenshaw notes the frequently associated endocrine disorder of Fröhlich type obesity. There is a tendency for the condition to become bilateral. Aching and limping may precede the clinical deformity by a few weeks to two years, but radiographic evidence of partial displacement is usually not long delayed. Cases in which the displacement is slight are in danger of being missed. This is especially important since prompt treatment saves the joint from possible late arthritic damage.

Treatment of early cases in expert hands is very satisfactory. Union

Fig. 510.—Infantile Coxa Vara.

Radiograph showing: (1) A clear area in the neck of the femur, quite distinct from the epiphyseal line, and distal to it. (2) The presence of a fragment of bone in the lower part of the clear area, the shape of this fragment being that of an inverted V. (3) A shortened neck. (4) Decreased angle between neck and shaft. (5) Some translucency of the femoral head.

(By courtesy of Mr. R. Ollerenshaw, F.R.C.S., and *Proc. roy. Soc. Med.*)

occurs by bone after satisfactory position and resultant shortening is very small. Absence of adequate treatment leads to gross deformity and necessitates osteotomy.

The femoral epiphysis may become separated in osteomyelitis, septic arthritis and tuberculous disease. Renal rickets should be suspected and certainly excluded in a bilateral case. Coxa vara, due to general bone disease, may be seen in rickets, chondrodysplasia, achondroplasia and fibrous dysplasia.

Coxa Valga

Coxa valga is relatively rare. It is most often seen in cases of paralysis or disuse of the lower limbs and for various reasons when one or both legs have not borne the body weight, *e.g.* unreduced congenital dislocation of

the hip ; fragilitas ossium : infantile paralysis, and rarely from a slipping upwards of the femoral epiphysis. In coxa valga of marked extent subluxation upwards may occur.

Protrusio Acetabuli

Otto in 1824 described the condition of acetabular protrusion in which the convexity of the acetabular walls project into the pelvis and may occur as a result of trauma, or acetabular sepsis, and very rarely as a congenital malformation. Verrall has called it arthrokatadysis.

Jones (1940) reports such a case in a girl aged twelve-and-a-half years with pain in the hips, great difficulty in walking, movements at each hip

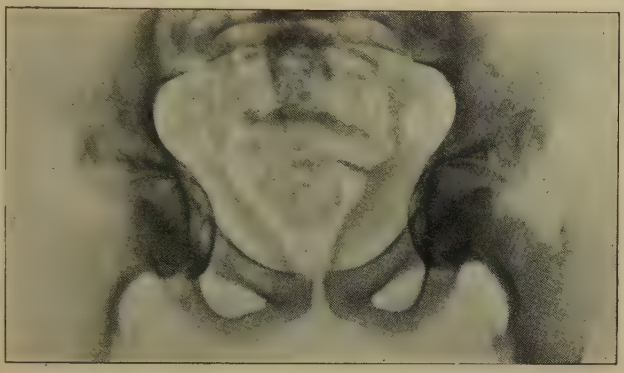

Fig. 511.—Protrusio Acetabuli.

Radiograph of a female child aged twelve and a half years. First came under observation at the age of twelve and a half. The acetabula project somewhat deeply into the pelvis ; the joint space is well preserved in each hip and there is no evidence of arthritic changes.

(By kind permission of Mr. A. Rocyn Jones, F.R.C.S., and *Proc. roy. Soc. Med.*)

greatly restricted with very little flexion and abduction, no adduction, internal rotation or external rotation, and a lumbar lordosis. X-ray examination showed deep acetabula, the floors of which projected into the pelvis, but the joint spaces were well-preserved (fig. 511).

The walls of the acetabulum may be so softened and plastic for a time after hip injury, or neighbouring sepsis, that the femoral head perforates to a varying degree into the pelvis and this is particularly demonstrated by Ghormley.

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OSTEOCHONDRITIS JUVENILIS

This is an important and relatively common type of bone disease in children. There seems to be no doubt that the lesions described by various writers are manifestations of the same fundamental process modified by local factors in different sites. The lesion at the upper end of the femur was described by Perthes in 1910, that of the tubercle of the tibia in 1903 (Schlatter and Osgood), the apophysis of the os calcis (Haglund, 1907 and Sever, 1912), the tarsal scaphoid (Köhler), the metatarsal heads (Freiberg), the vertebral bodies (Scheuermann), and there are other accepted sites of the condition.

Ætiology.—Heredity is not a factor and the child is usually otherwise healthy. No wholly satisfactory cause is known, but opinions include the possibility of trauma, vascular or neurotrophic disturbance, mild chronic infection and aseptic necrosis.

Pathology.—The description by Mills epitomizes the subject and states that the bony nucleus concerned first appears irregular in outline with sometimes an eroded surface whilst there may be local areas of rarefaction in the neighbouring diaphysis. The nucleus becomes strikingly flattened as though crushed in the normal line of pressure, and at the same time it becomes very much denser. This compression with increased density is a striking feature and may be extreme ; in the tarsal scaphoid the shadow may so simulate radiographically a metallic body. The nucleus frequently breaks up into two or more fragments and the line of the neighbouring joint is often blurred. The joint space is always clear and may be wider than normal during earlier stages of the disease.

As recovery occurs the density diminishes, the bone structure again becomes visible and reconstitution proceeds, the joint space is clearly defined and there remains only a degree of deformity, which varies inversely with the amount of protection given during the active period of disease. It must be understood that the affected bone soon becomes plastic and remains so through the various degenerative and regenerative phases ; thus compression deformity is possible from adjacent bones. Abscesses never occur. Recovery proceeds without ankylosis.

Pseudo-Coxalgia

Synonyms.—Calvé-Legg-Perthes disease, Osteochondritis deformans juvenilis, Coxa plana.

In 1909 and 1910 appeared three articles, one by Legg in America, another by Calvé in France, and a third by Perthes in Germany, calling attention to an affection of the hip-joint which had previously been included among the tuberculous hips but presented distinguishing features, the chief of which were the remarkable recovery of movement and function, and the characteristic radiographic changes. The most marked of these changes affect the ossific centre for the head of the femur, and are quite different from those associated with tuberculosis. It affects active vigorous children of both sexes, but more commonly boys, with no sugges-

tion of a tuberculous infection. A history of trauma is common. It usually affects one hip, but may be bilateral.

Morbid anatomy.—Since operation is contra-indicated in this affection pathological material is scarce. Phemister examined a portion of the femoral epiphysis removed at operation, and described the microscopical appearance as typical of an old infective lesion. In two reported cases staphylococci were grown from the debris removed from the neck of the bone. The view that receives some support at the present time is that the changes are due to an infective process though others cling to the traumatic theory.

Clinical picture.—A healthy looking boy, between five and nine years of age, limps and perhaps complains of pain in one hip. Examination reveals a little thickening about the neck of the femur, and limitation of movement in certain directions. In a typical case abduction is most limited whereas flexion remains surprisingly free—a noteworthy picture. Rotation, particularly internal rotation, is not uncommonly limited. Shortening is absent in the early stages, and never amounts to much, half an inch at the most, even at the termination. The radiographic changes vary with the particular stage at which the patient is examined, but X-ray examination is always essential to confirm the diagnosis, and sometimes affords the only certain evidence. If a case is seen in the early stages and X-ray pictures are taken periodically during the next two or three years, the following changes can be noted (fig. 512 and 513). At first the only abnormality is a slight widening of the joint space and a slight flattening of the convex surface of the epiphysis. Later, the epiphysis is more flattened, and denser than normal. Clearer areas now appear in it, which extend until it is broken up into separate pieces (fragmentation), whilst it has extended somewhat in the lateral direction beyond the limits of the neck. The neck is a little rarefied and sometimes shows well outlined clear spaces which differ from tuberculous foci in being much more clearly defined. The ossification of the head now begins to improve, new bone being deposited so that the fragments all coalesce until eventually the head appears to be more or less of normal shape and density. Rarely is restoration towards the normal quite complete. In most cases the reossified head is shallower, and more spread out than the normal; or the head remains mushroomed; the cartilage remains intact but is moulded to some extent by pressure to conform to the altered shape of the ossific centre. Cases have been reported of one or more fragments of the epiphysis remaining separate and even forming loose bodies, in which case there must be a breach of the cartilage. The acetabulum not uncommonly shows some irregularity, and may be shallower and wider than normal. There is also a condition of ischium varum described with this widening.

As to clinical signs, these eventually clear up, but the limitation of abduction and the limp may remain for several months. At any period in the course of the affection spasm of the muscles about the joint may supervene so that all movements become limited or obliterated. When this spasm is present a diagnosis from tuberculosis can only be made with certainty by radiographic examination. Abscesses do not form.

Prognosis is always good. In some cases, however, the head of the femur remains more or less mushroomed, a condition which favours the onset of chronic arthritis (osteo-arthritis) later (Eyre-Brook).

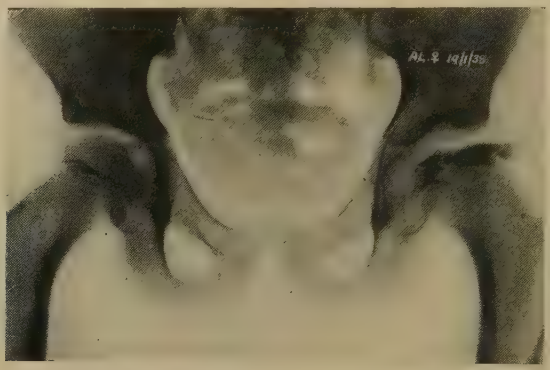

FIG. 512.—ACTIVE PHASE OF LEGG-PERTHES DISEASE OF THE FEMORAL CAPITAL EPIPHYSIS.

FIG. 513.—SAME CASE FIFTEEN MONTHS LATER SHOWING FURTHER COMPRESSION OF PLASTIC BONE AND SOME ABSORPTION OF CALCIUM.

(By kind permission of Dr. James F. Brailsford and the *Brit. J. Surg.*)

Treatment.—This varies with the clinical signs. If spasm is present, the hip should be treated by immobilization and extension for a few weeks. If these arthritic symptoms are absent, the period of recumbence may be dispensed with. A weight-bearing caliper splint may be worn, with the

necessary adjustments from time to time, until radiographs show the affection to have run its course. It may be considered doubtful if a weight-bearing splint can give sufficient relief from weight bearing to achieve the desired end.

Some surgeons believe that the course is unaltered by treatment and that the latter is superfluous, but it is rational to think that relief from weight bearing must diminish the moulding of the cartilaginous head that takes place while the ossific centre is partially decalcified. Recumbence and prolonged weight extension is now used more frequently than formerly in the hope of preventing permanent deformity of the femoral head. It should be understood that the ossific tissue in the femoral head is in a plastic state for a long time, often eighteen months, and in extreme cases up to four years, so that in order to avoid insidious deformity prolonged supervision is necessary.

Osteochondritis of the Spine

This spinal affection is seen at least as often as the femoral type ; some would say it is even more often seen. The disease may affect several vertebræ, most commonly in the lower dorsal or the dorso-lumbar region, not necessarily contiguous, and usually produces a general exaggeration of the dorsal curvature. Gross changes may occur in the lumbar spine even without symptoms. In advancing cases a wedge-shaped deformity of the vertebral bodies and diminution in thickness of the disc occurs. The upper and lower margins of the bodies show irregular outline suggestive of erosion, and the metaphyseal zone appears splayed out. The epiphyses may show added density, thus giving an area of transparency between the epiphyses and the body. Ultimately a considerable amount of the vertebral body may be involved in the destructive process. Fragmentation of an epiphysis may occur. Kyphosis or scoliosis may develop. The disease occurs more frequently in rapidly growing children round ten to sixteen years of age. Dorsal kyphosis is detected ; slight pain, local tenderness, stiffness or weakness in the back is mentioned in the typical case. Muscular spasm and limited movement are not conspicuous. Flexing the spine is often easily performed, and produces a humplike deformity. Spinal rotation is practically normal, but extension is obviously limited even in early cases. Diagnostic confusion with tuberculous spine is possible especially when one vertebra is affected, but fine radiography usually clarifies the doubt. In order to avoid the remote effects and deformity of compression and sclerosis of the bone and secondary ossification of local ligaments, recumbent treatment of the early condition before the plastic vertebral bodies have been compressed is indicated. In fact recumbent treatment is the only treatment that is effective and should be followed up by a back support and exercises.

Osteochondritis of the metatarsal region usually affects the head of the second metatarsal and causes local pain and definite tenderness. Swelling is generally present but joint movements are free.

Osteochondritis of the tubercle of the tibia is indicated by slight

prominence and local tenderness, and radiographically the epiphysis appears to be moved away from its attachment to the shaft (fig. 514).

Osteochondritis of the capitellum.—A boy aged eight years complained of inability to bend his elbow. He had been injured by a stone two

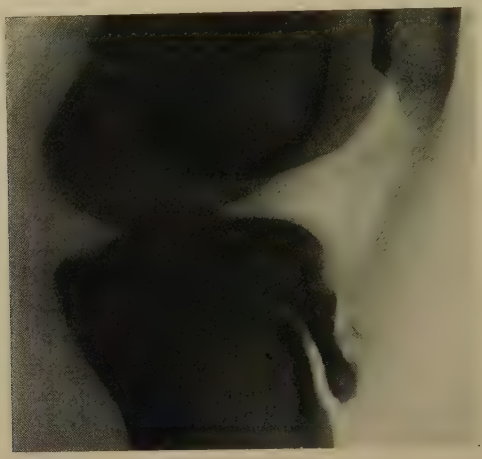

Fig. 514.—Osteochondritis (Schlatter's Disease).

months previously. He had full extension, pronation and supination, but flexion reduced to a right angle. Radiography showed typical osteochondritis with fragmentation of the capitellum. Two years later the capitellum had reformed and full range of movement returned (Malkin). In this condition a loose body may form and be associated with a click on movement or even locking.

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Spondylolisthesis

The name spondylolisthesis is descriptive of a "gliding vertebra" leading to forward subluxation of the body of one of the lower lumbar vertebræ on the vertebra below it, or upon the sacrum. The fifth lumbar vertebra is the one usually displaced. The malposition may be slight

or considerable. The displaced vertebra may also be somewhat rotated on a transverse axis. The cause is often obscure; trauma, not necessarily severe, may be related, but an anatomical weakness between the vertebral laminae and the bodies is suspected to be essential to the condition. Congenital defect or abnormality in the local vertebral development, preceding the deformity, may be detectable. Brailsford suggests that a process akin to osteochondritis, with softening of the pedicles, and

FIG. 515.—SPONDYLOLISTHESIS.

Girl aged nine years. No history of injury. Essential symptoms were inability to run about easily. She could not fully extend the left thigh when lying flat. Radiographs showed characteristic changes.

perhaps induced by trauma early in life, may be concerned in the process. It is by no means an uncommon condition in adults, but it is rarely seen in childhood.

Clinical symptoms and signs.—There may be local pain or dull ache in the lower back and some limitation of movement in the lumbar region. The posture is affected and possibly pain referred by local pressure on nerve roots.

On inspection of the back, the spine curves forward sharply above the sacrum giving an apparently increased lumbar curve and the upper spinous processes of the sacrum give a kyphotic appearance. The trunk appears to be shortened.

Radiographically there is an abnormal forward projection of the displaced fifth lumbar vertebra, and the sacrum appears to be pushed backwards. Viewed from above the anterior surface of the fifth lumbar vertebra has a bow outline.

The patient is generally in good health, otherwise, but there may be limited extension of one or both thighs. In a case recently seen, in a girl aged 9 years, full extension of the left thigh could only be produced by allowing spinal flexion, there was some wasting of the buttocks and tingling pain felt in the foot, as a result of pressure on the cauda equina.

The condition must be clearly differentiated from local deforming tuberculosis, osteochondritis, or acute fracture dislocation. Treatment is essentially by orthopædic methods, using special extension frame, followed by lumbosacral fusion. A case with excellent results is reported by Spray and Ghormley.

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SYPHILITIC DISEASE OF BONE

Although infants may acquire syphilis, the cases seen in practice are nearly always congenital; the following description will therefore deal with that form.

The bony lesions of congenital syphilis, which have been stated to be as frequent as the cutaneous manifestations, differ somewhat from those of the acquired disease in adults. This is connected with their occurrence during the period of growth of bone, for the syphilitic changes are most marked at the epiphyseal ends of the long bones and the centres of ossification of the flat bones of the cranial vault. The bones formed in cartilage are affected earlier than those laid down in membrane; thus, syphilitic disease of the epiphyses (osteochrondritis) has been seen in stillborn infants, whereas the nodes on the cranial bones occur later.

Syphilitic epiphysitis.—Synonyms.—Osteochondritis (Wegner), Parrot's disease.

This is a lesion of very early life, generally within the first three months, and may be present in stillborn infants. It is said to occur in 5 per cent. of infants with congenital syphilis (Milan), but other estimates are much higher. Frequently several members of a syphilitic family are attacked, thus illustrating the liability of certain tissues in such families to be specially affected (Thomson).

Morbid anatomy.—There is syphilitic inflammation of the epiphyseal plate of the metaphysis, and of the overlying periosteum; the epiphyseal plate becomes swollen, yellowish-white, and the process of ossification irregular. The so-called separation of the epiphysis, which is not uncommon, is really a misnomer, since the separation always occurs as the result of softening of the diaphysis a short distance from the

epiphyseal plate, as may be demonstrated quite clearly in X-ray pictures. The treponema pallidum cannot always be demonstrated in typical cases of epiphyseal disease (Schultz). Either or both extremities may be attacked, the upper end of the humerus and the region of the elbow joint being most often affected perhaps. Usually it is symmetrical, though one side may be more markedly affected. Periostitis over the ends of the bones and also along the shafts, particularly of the short long bones, may occur without epiphyseal disease. It is common to see, in an X-ray picture, subperiosteal shadows in relation to the metacarpals and phalanges.

Fig. 516.—Syphilitic Osteo-periostitis.

Girl aged three years. Swelling right leg—noticed at the age of nearly three years. No other objective signs of specific disease. Fusiform, hard, non-fluctuant, tender swelling palpable in the lateral aspect of the calf. Wassermann reaction positive. Very satisfactory response to anti-specific treatment.

Clinical aspect. — The infant never moves the affected limb voluntarily, and cries when the part is manipulated, though there does not appear to be any pain at other times. The limb is flaccid and flail-like, but the muscles react to electrical stimulation, and there is no true paralysis. This pseudo-paralysis, which may occur without any evidence of epiphyseal disease, is, in the absence of rickets, characteristic of congenital syphilis. There are usually swelling and slight œdema at the site of the lesion. When separation of the epiphysis has occurred, there may be crepitus, but this is far from constant.

X-ray examination shows rarefaction of the diaphysis and the separation of the epiphysis, together with a small portion of the diaphysis (fig. 516). Union takes place readily under appropriate treatment.

Prognosis is favourable when one or two bones only are affected, and when appropriate treatment is adopted. In many cases there is complete restitution of the bone, but the outlook is not so good when the lesions are multiple and when other syphilitic manifestations are severe.

Diagnosis.—Signs of syphilis elsewhere, a positive Wassermann reaction, both of the child and the mother, and to a lesser degree pseudo-paralysis, make the diagnosis certain. The epiphyseal enlargement might be confused with that of rickets, in which pseudo-paralysis may

also occur; the concomitant signs of the two diseases should prevent mistake, but the two diseases may co-exist. As a rule, however, the syphilitic lesions appear much earlier than rickets. It must be distinguished from traumatic and other forms of acute arthritis, especially of gonococcal or pneumococcal origin, and multiple arthritis, due to pyæmia.

Infantile scurvy produces a swelling which is not confined to the epiphysis, is accompanied by some other diagnostic signs, and hardly ever occurs before the age of six months. Birth palsies do not implicate the joints, and are present at birth. Acute poliomyelitis also does not involve the joints, and is not always painful on movement.

Other bone affections.—The *skull* in early congenital syphilis is affected in one of two main forms: (1) atrophic, in which absorption of bone occurs. In addition to craniotabes or discrete areas of atrophy there is in rare instances more widespread absorption of bone (caries sicca). The bones of the nose commonly undergo syphilitic ulceration. (2) Hyperplastic, in which there is thickening of the bones of the cranial vault, giving rise to the well-known Parrot's nodes or the natiform or hot-cross-bun skull. When there is rickets in addition, as is not uncommonly the case, the new bone is soft in consistency (Shattock). In cases of combined syphilis and rickets the bossing of the skull is more marked than in either disease alone. In both craniotabes and bossing of the skull the relative importance of syphilis and rickets has been much discussed. The cranial bossing may be associated with some hydrocephalus and distension of the cutaneous veins.

Syphilitic dactylitis is not common; in one hundred cases it was noted in two (Still). It usually occurs within the first two years of life, and has been seen a few months after birth. It attacks one or more bones, generally the proximal phalanges of the hands, and may be symmetrical, the swelling being more noticeable on the dorsal than on the ventral surface. Doubt exists as to the morbid anatomy; some describe it as a gummatous periostitis, others as epiphysitis, and others, again, as an osteomyelitis. Possibly the morbid change is not the same in all cases. It resembles tuberculous dactylitis, but is less prone to attack the metacarpals, and does not give rise to pain or suppuration. The treatment is the same as in the early stage of congenital syphilis.

In delayed congenital syphilis bony changes are frequent. In 132 cases the bones were affected in 39 per cent., the liver being the most frequent site of lesions—namely, in 34 per cent. (Forbes). The bony changes are most often seen at and shortly after the age of five years, and become less frequent at the age of fifteen. The disease attacks the long bones, and particularly the tibia. Usually more than one bone is affected, and not uncommonly the disease is symmetrical. There may be nodes on the long bones, particularly the tibiæ, resembling those in acquired syphilis. In a rather special form of the disease the changes consist of hypertrophic osteo-periostitis, with extensive production of new bone, or there may be gummatous formations in the medulla and other parts of the bone, or the same bone may show combined osteo-

periostitic and gummatous changes. A gumma may cause spontaneous fracture, but this is rare. The usual change is chronic or subacute osteo-periostitis, and may lead to such hyperostosis that osteitis deformans or a sarcoma is simulated. The tibia becomes bowed forward (sabre-blade tibia) and at first sight the real curving in rickets is simulated; but the middle third of the bone, instead of the lower third as in rickets, is mainly affected, and radiography shows absence of the characteristic rickety deformity. As the result of the hyperplastic process, the length of the bone is increased. Necrosis and suppuration, probably due to secondary infection, may occur. Pain, especially at night, may be the earliest manifestation; it may be severe or may be almost absent. In some instances the patient shows infantilism or progressive mental enfeeblement; occasionally, as the result of syphilitic endarteritis, the pulse may be absent from the extremities, and symmetrical gangrene suggesting Raynaud's disease may occur. Keratitis is commonly associated.

Diagnosis.—Evidence of syphilis elsewhere or a positive Wassermann reaction may clinch the diagnosis. The condition must be distinguished from the lesions of rickets by the points already mentioned and by other symptoms. Typhoidal and staphylococcal periostitis may occur in children, and will be suggested by the history and by the absence of other signs of syphilis.

Treatment.—Anti-syphilitic treatment should be employed, but the massive osteo-periostitis may be very resistant to treatment. Whilst penicillin appears to be most effective in the more severe cases of congenital syphilis, in the infant, the osseous changes do not always appear to respond adequately. Therefore if penicillin is used in this disease it should be followed up by other anti-specific remedies (ch. XXXIV).

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Sarcoidosis

Boeck (1899) described the clinical picture and microscopical structure of a characteristic skin affection to which he gave the name of "benign sarcoid." He also observed similar nodular lesions in the viscera. Schaumann (1914) confirmed and enlarged the conception of Boeck and also noted that histologically the sarcoid consisted of epitheloid cells, lymphocytes, a few giant cells, and later intense sclerotic fibrosis. Caseation and calcification are always absent. The disease may present a number of different syndromes because dissemination of the sarcoid may take place in the skeleton, and in mucous membrane, lymph glands, lungs, myocardium, iris and salivary glands, liver and spleen and produce

general symptoms of recurrent fever. Heerfordt's disease, "uveoparotid fever," may occur.

The reticulo-endothelium of the bone marrow is a site of predilection for sarcoid and the characteristic bone lesions nearly always develop in the phalanges of the fingers and toes. The digit affected shows cyanosis and fusiform swelling and red-blue discoloration somewhat resembling tuberculous dactylitis. Malformation of one or more fingers and dystrophic changes of the nails may be present; associated lesions of lupus pernio of the skin of the hands and feet would suggest the clinical diagnosis of sarcoid. X-ray examination shows three different types of bone lesions: (1) multiple circular punched out areas of bone resorption in the phalanges, sometimes in the metacarpals and metatarsals. The bony tissues surrounding these areas does not show any reaction such as bone atrophy or sclerosis; (2) sometimes the bone structure of the phalanges is modified by a more generalized dissemination of groups of sarcoids, giving a lattice aspect; (3) in other cases dissemination of isolated sarcoids occurs in the reticulum of the bone marrow, the lesions being too small to be distinguished by naked eye and so giving an X-ray appearance of general atrophy of the skeleton of the hands and feet. The course of the skeletal lesions is slow. After many years the bone and skin symptoms usually disappear spontaneously. However, even when the fingers have become visibly normal X-ray examination may still show last remnants of the bone lesions. Minute cysts may be seen as a relic of previously active lesions. Sarcoid disease may be apparent elsewhere and possibly be shown by swelling of lymph glands especially at the lung roots, lung infiltration, enlarged liver and spleen, nodular iridocyclitis; fever, leucopenia or moderate leucocytosis, and increased sedimentation rate are usually present. Tuberculin reactions are usually negative. Biopsy of a suspected skin sarcoid may be helpful. The sedimentation rate is increased in the active stages and the globulin content of the blood may be raised. Prognosis is usually favourable. Even extensive signs may disappear under observation and complete cure occur. This remarkable disease is considered to be a peculiar reaction of the reticulo-endothelium with formation of pseudo-tubercles under the influence of an unknown virus. Pulmonary sclerosis may cause death. Treatment remains purely empirical; general hygienic and dietetic care, arsenic, large doses of ascorbic acid and various radiations have been recommended, but none have been proved to be of genuine value. Gold salts, *e.g.* sodium aurothiomalate, have been used in the treatment of this disease.

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Craniotabes

This term has been applied to more than one condition, but this description will be confined to localized spots of thinning of the cranial bones—the craniotabes of Elsaaser (1843). These may be due to several causes, the relative influence of which has been variously estimated. They are commonly due to marasmus, and accompany rickets or are due to dietetic errors which later induce rickets (Cautley). Syphilis is a factor of importance. According to Barlow and Lees, 47 per cent. of the cases of craniotabes are syphilitic, and Carpenter found that, out of 238 cases of craniotabes, 204 or 87 per cent. were syphilitic, that 61 per cent. occurred within the first four months of life, that is before rickets is an active factor—and that about 50 per cent. of syphilitic infants show craniotabes. The most marked examples are seen in children with both rickets and syphilis. Craniotabes may occur in chronic hydrocephalus, and may be met with in infants in whom no obvious cause is forthcoming.

The parietal and occipital bones are affected. In 60 per cent. of Carpenter's cases the parietals alone were affected, and in less than 3 per cent. was the thinning confined to the occipitals. Adami figures craniotabes in the frontal bone. These areas are chiefly seen near the lambdoid suture. The thinning has been thought to be due to the pressure exerted on mal-nourished bone by the pillow on the outside, and by the brain internally. The process of bony absorptions begins in the inner table and may advance so much that only a layer of membrane is left. These thinned areas, which can be well seen by holding the skull-cap to the light, yield when pressed by the finger, and feel like tightly stretched parchment. Craniotabes is not uncommonly associated with laryngismus stridulus, both being manifestations of rickets. Osteogenesis imperfecta can be easily distinguished. Cranial xanthomatosis gives distinctive radiographic appearances.

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Bossing of the Skull

Bosses on the bones of the vault of the skull may be associated with several conditions, especially with rickets and inherited syphilis; in fact, the most marked examples are found in patients with rickets and syphilis combined. These bosses are due to the exuberant formation of new bone around the centres of ossification of the frontal and parietal, and occasionally of the occipital and temporal bones. Usually the bosses are symmetrical. *Plagiocephaly*, or a prominent boss on one half of the frontal bone, usually the right, with a corresponding prominence on the opposite occipital region, may depend on the position of the child's head

during the later months of fœtal life. As a result of the heaping up of bone over the frontal and parietal eminences, the lines of the sutures appear depressed, and the well-known natiform or hot-cross-bun skull results. It has been stated that when due to uncomplicated syphilis, the bosses are nearer to the anterior fontanelle than are the bosses due solely to rickets ; but clinically it is unwise to attempt any such distinction purely on the position of the bosses. Other evidences of syphilis or rickets in the head and elsewhere in the body must be sought for. These bosses, specially described by Parrot, are often called " Parrot's nodes." As is well known, he considered that rickets was due to inherited syphilis, a view which has never been accepted in this country. Bossing of the skull may occur in cases of anæmia with splenomegaly, and may then be due to associated syphilis or rickets.

Osteo-periostitis over the centres of ossification of the frontal and parietal bones may be due to tuberculosis, and may for a time imitate syphilitic disease. As many as twenty-nine such bosses have been recorded in a child aged two years (Ménard and Bufnoir). They may suppurate, and a diagnosis of their nature may be made by the detection of the tubercle bacillus.

Bosses on the bones of the vault also occur in achondroplasia, hereditary cleido-cranial dysostosis, secondary metastases of new growth, for example, in malignant hypernephromata and chloroma.

In infantile scurvy bosses on the skull may be due to concomitant rickets or, in rare instances, to hæmorrhages. Bosses in the temporal regions with displacement of the ears occur in osteogenesis imperfecta (H. C. Cameron).

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Leontiasis Ossea

Synonyms.—Hyperostosis cranii, general hyperostosis, cephalomegalia.

This is a rare disease found usually in younger individuals and producing diffuse hyperostoses, starting in the bones of the face and extending to the skull. As a result the face ultimately becomes ogre-like. Finely porous bone thickenings transform to a marble hard form. The bosses of abnormal bone are usually irregular in extent and distribution, the forehead, skull base, superior maxilla and the mandible showing asymmetrical development. The facial cavities and cranial foraminæ become narrow and the skull heavy. Facial deformity may reach bizarre degrees with an unchangeable masklike appearance, although mental status may be unimpaired for many years. Brailsford (1944) describes a child aged six years in which the early radiographic signs were thickening in the region of the frontal sinus ; X-ray pictures taken one to three years later showed the frontal bone one inch thick and marked headaches were present. The disease is slowly progressive but repulsive facio-cranial deformity is usually not apparent during childhood.

Knaggs considers two groups of cases: (1) those with chronic periostitis, and (2) those with diffused osteitis of the bones of the face and skull. Some remarkable examples of combined facial and dental hemihyperplasia are noted by Rushton.

Ætiology.—According to Hallé in 1912 there were only thirty cases on record. It appears that about a third of the cases start in childhood, and according to Apert and Bordet, usually between the fifth and ninth years. Out of twenty-eight cases collected by Kanavel nine were congenital or began in early childhood. Heredity does not exert any influence; the sexes are equally affected.

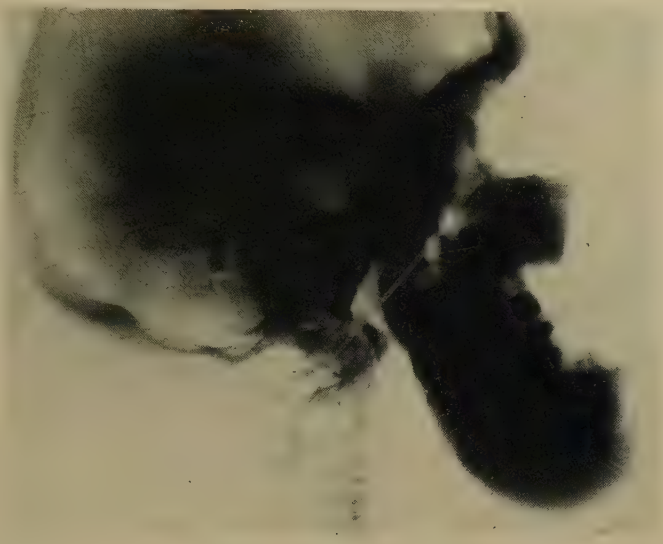

Fig. 517.—Leontiasis Ossea.

The cause is unknown. It has been suggested that it is a trophoneurosis, but there is no evidence of any primary change in the nervous system. Fairbank regards leontiasis ossea as being indistinguishable from the hyperostosis of the skull seen in cases of polyostotic fibrous dysplasia.

Morbid anatomy.—All the bones of the head—cranial and facial—are affected. There is great thickening, which leads to obliteration of the various air sinuses, to narrowing of the foramina for nerves and vessels, and to diminution in the size of the orbits. The change is generally described as hyperostosis. The essence of the condition is the formation of fine cancellous bone in the spaces filled with fibrous tissue; and this is sometimes associated with diffuse fibrosis of bone in other bones in the same side of the body.

Symptoms come on earlier and are more prominent than in ordinary osteitis deformans. The skull, and especially the forehead, increase in size. The early symptoms are headache, paroxysmal and often frontal

and an increase in the size of the skull especially bulging of the forehead. Optic atrophy, deafness, anosmia, and cranial neuralgias may result from foraminal narrowing and basal sclerosis, whilst distension of veins, embarrassment of the cerebral circulation and mental disturbance result from narrowing of the channels for blood vessels. Exophthalmos and downward displacement of the eyeball are often present. The course of the disease is slow, and may be prolonged for twenty or thirty years.

Diagnosis.—The condition must be distinguished from acromegaly, with which it has in the past been confused. Hyperostosis of the skull and other bones may occur after the arrest of severe rickets. A form of bone disease resembling osteitis deformans, and chiefly seen in the tibiæ, may be due to congenital syphilis.

Treatment.—Anti-syphilitic treatment should be given a trial. If this fails, surgical treatment may occasionally give relief.

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Hyperostosis Frontalis Interna

This is essentially a disease of adults but two cases in Moore's extensive series were older children and several were recognized in late adolescence. Female cases markedly predominate. The essential cranial change is a nodular, sessile or mixed hyperostosis of the frontal bone and possibly also the orbital plate. The hyperostosis diminishes as it recedes from the mid-line. There is no change in the external surface of the outer table of the skull. Through its physical characteristics, this condition is quite distinct from bone tumour, osteitis fibrosa and leontiasis ossea. It is associated with a variety of possible symptoms—psychic disorder with intellectual slowness, change of temperament and character, headache with paroxysmal exacerbations, obesity of the hypophyseal genital type sometimes reaching extreme degree, polyuria, cranial nerve (2nd, 7th and 8th) compression, and sleep rhythm disturbance. Hypercalcæmia has been found, but is not constant. Although the hyperostosis is the pathognomonic sign, it probably is only an associated effect of a complex neuro-psychiatric disorder.

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NEW GROWTHS OF BONE

Non-malignant new growths.—Simple cysts of bone are not common; they chiefly occur during the period of growth and at some little distance from the ends of the long bones, especially the femur, humerus, tibia, and fibula. Bloodgood collected thirty-six cases under fifteen years of age. They have been thought to be due to injury, but appear to be closely connected with fibrous osteitis, and may be due to softening of a patch of fibrous osteitis. Pain is usually absent, and fracture of the bone may be the first sign, but the subsequent union may be satisfactory. These cysts, by radiography, show a hollow cavity with a regular outline. The swelling should be explored and the contents examined microscopically. When, however, a fracture occurs through a cyst, time should be allowed for union to take place before resorting to operation. In the case of cysts of moderate size consolidation and cure of the cyst may occur as callus is formed, and operation may prove to be unnecessary. Elmslie recommends curettage with crushing in of portions of the cyst wall. Bone graft may be inserted after clearing the cyst, to hasten the consolidation.

The so-called "*myeloid sarcomata*" (osteoclastomata), which arise endosteally from the spongy tissue at the ends of the long bones, and most frequently in the upper end of the tibia, are locally destructive, but not truly malignant. They are commoner after the age of twenty years, whereas simple cysts are more frequent under that age.

The contents of the bone cavities may be largely or wholly fibrous tissue, and not for the most part fluid, or the fusiform enlargement of the bone may consist of cancellous tissue, the spaces of which are filled by a cellular fibrous tissue (osteitis fibrosa), without any major cavitation or cysts.

This condition of *fibro-cystic disease* may effect one bone or many. The multiple cases fall into two groups, the multiple focal type with no disturbance of calcium metabolism, and generalized fibro-cystic disease (von Recklinghausen) with marked increase of the blood-calcium and of the excretion of calcium in the urine and fæces. These multiple cases are rare and particularly rare in children, but the number of cases reported since the observation and researches of Erdheim, Mandl, and of Collip were published is mounting up and knowledge of them is increasing, largely owing, in this country, to the work of Hunter. The latter group is now known to be associated with over-secretion of one or more of the parathyroid glands, the result of a true functioning hyperplasia. The bones, in response to the increase in the parathyroid secretion, become decalcified, the amount of the blood calcium being increased while an excessive amount is excreted. Pain and fragility of the affected bones are marked features of these cases. It is important to note that there is a generalized osteoporosis of the skeleton and that the fragility is not confined to the bones with cysts. Exploration of the neck and removal of the offending parathyroid gland results in rapid relief of pain and gradual improvement in the osseous and general

condition of the patients. In the former group, the "multiple focal" type, bio-chemical investigations reveal no sign of calcium inbalance and exploration of the neck is not indicated. Fairbank met with two cases in children, in whom the bone changes were practically confined to one side of the body. In one of these, under the care of Barrington-Ward, the temporal region of the skull on the same side as the cysts was the seat of "leontiasis." In these two cases there was no definite disturbance of the calcium metabolism and they probably represent examples of fibrous dysplasia of bone. Cyst-like areas are seen in the bones in some cases of lipoidosis; the clearest example is that of osseous xanthoma.

Osteoma.—In childhood an osteoma is always near to and probably arises from the epiphyseal cartilage as a form of chondrodysplasia. The tumour continues to enlarge until epiphyseal union takes place. There is a covering of cartilage and the cancellous bone is in continuity with the parent bone. Multiplicity and some degree of symmetry is the usual pattern and their shape is variable; their disposition is common near the knee; adventitious bursæ may appear. Malignancy is so rare a complication that removal is unnecessary except to remedy pain, mechanical disability, nerve or vessel pressure, or unsightliness.

Chondroma.—Similarly to osteoma, chondroma may be situated near the ends of long bones, but they are more generally found in the long bones of the hands and feet, wherein they are usually multiple, and which, by outward growth from the medulla, cause nodular tumours and medullary distension, enchondroma. Secondary myxomatous and calcific changes may occur. Single chondroma at the end of a long bone, *e.g.* humerus—may slowly become quite large and show radiologically ossific changes or possibly rapid enlargement and clinical features suggesting sarcoma development. Simple chondroma may possess islands and branching areas of calcification.

A boy had a swelling in the upper portion of the right leg. X-rays showed a large oval swelling in the upper 7 inches of the right tibia. At operation the femoral vein was found to contain a column of cartilage, and microscopically the tumour consisted of hyaline cartilage with extensive areas of necrotic degeneration. Nine months later the boy was in excellent health.

Chondroma may arise from a vertebra and cause spinal compression or from the pelvic synchondroses and displace viscera. Scapular chondroma is regarded with special suspicion respecting sarcomatous metaplasia. Surgical removal of a chondroma is usually successful but in some cases recurrent tumour develops which may prove of changed structure (Neale, 1931).

Osteoclastoma.—This is ordinarily considered to be a benign tumour with uniform clinical and pathological features, and it must be regarded as a rare tumour in childhood. Microscopically it is a soft friable maroon-coloured tumour with fairly well defined edges. It grows slowly and there may be a history of local injury. The most common sites are the juxta-epiphyseal areas at the lower ends of the femur, radius and tibia and upper end of the tibia or fibula and the jaws. Osteoclastoma usually

involves the epiphyses, or what were epiphyses before they joined the shafts, whereas cysts quite definitely do not involve the ends of the bones, but grow on the shaft side of the epiphyseal lines. Radiologically their recognition is usually clear, but some difficulty may occur when the tumour is in an unusual place, *e.g.* vertebra, scapula, pelvis or smaller long bones. The tumour may not be limited by the epiphyseal line and so may penetrate to the articular cartilage. Clinically the tumour may cause little disability and be unrecognized until a fracture occurs. Pain is inconspicuous. Very occasionally liquefaction of the mass, inside the bony shell, takes place, and a blood cyst is simulated with only traces of the original tumour in evidence. The swelling remains well defined, with possible late disturbance of the nearby joint. Muscles or tendons are free. Palpable crackling may be detected over the thinned egg-shell like envelope.

The available evidence now concludes that in rare cases it is actually malignant; a few authentic cases are reported in which pulmonary metastases have developed. Also true sarcomatous metaplasia (xanthosarcoma, myxosarcoma, or spindle cell type) may be suspected from yellowish or pale and firmer areas of the tumour especially near the bony wall.

The true simple tumour may exist for years before detection so that the extent and site is such that local complete surgical treatment by scraping and chemical cauterization may imperil the joint. Brailsford puts forward a plea for X-radiation therapy, without previous biopsy as the treatment of choice. Operation in an advanced case leaves a very weak shell of bone which takes some months to strengthen, but bone graft should be considered. Blood calcium, phosphorus and phosphatase are normal. Osteoclastoma in a membrane bone is a clinical rarity.

One such case in the parietal bone of the skull has recently been seen by the writer. The child was aged $2\frac{1}{2}$ years. Her mother noticed a swelling $\frac{3}{4}$ inch in diameter on the surface of the skull. Examination four months later revealed a soft circular fluctuant swelling one inch in diameter, in the left parietal area. An incision showed a soft bluish-purple vascular tissue deep to pericranium. X-ray examination showed a local bone defect; the rest of the osseous system was quite normal. Section of biopsy tissue showed typical osteoclastoma. Shortly after, the whole tumour was eradicated and the bone around the defect nibbled away leaving the dura clean and intact.

Angioma.—Hæmangiomatous tumour formation may occur in one bone, *e.g.* tibia, vertebra, or mandible. In the latter site severe bleeding may follow dental extraction. Hæmangioma may involve the bones of an extremity. Radiologically the bone shows a relative osteoporosis with irregular areas of cancellous structure. Hæmangiomatous nævi may lead to local hyperostosis of the skull. Diffuse angiomatosis sometimes causes greater development in the bone of the affected limb. Hæmangioendothelioma may produce a cyst-like expansion of one or more bones. Generalized osseous and visceral angiomatosis, bearing clinical and radiological similarity to the osseous form of Gaucher's disease, is reported by Parsons and Ebbs.

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Multilocular cystic disease of the jaws.—Familial multilocular cystic disease of the jaws is the name which Jones (1933) used to describe an uncommon condition which he observed in four of five children in the same family. He considers the condition to be of the nature of multiple dentigerous cysts arising throughout the upper and lower jaws and presenting signs, towards the end of the second year of life, as bilateral painless

Fig. 518.—Multilocular Cystic Disease of the Jaws.

Three children of the same family, aged six, five, and four years, reading from left to right. Note the full rounded cheeks and jaws. The submaxillary lymph gland enlargement is well seen, being most marked in the two younger children.

(By kind permission of Dr. W. A. Jones and the *Brit. J. Radiol.*)

swellings of the jaw bones. In some cases enlarged submaxillary lymph glands are detectable, which on microscopic examination reveal a chronic hyperplastic inflammatory change.

The osseous abnormality proceeds at a variable rate, and ill-developed teeth are shed. The lower gum margin may show an epuloid thickening consisting of inflammatory granulation tissue. The blood has revealed no changes apart from, in some cases, a raised serum phosphorus.

Jones (1938) in a critical examination of serial X-ray pictures taken over a period of years, and the observation that the disorder spreads throughout the teeth-bearing areas, considers the essential process to be an anomalous development of dental structures. In no case has more than the normal number of teeth been present. Many of the cystic areas did, however, contain teeth which have erupted in an irregular manner.

Cysts, not containing teeth, extend into the rami of the lower jaw ; and

possibly cysts bearing no evidence of having contained teeth indicate an abortive attempt at multiple formation of teeth, the tooth buds having degenerated with cyst development. In one family the abnormality was traced through five generations.

Clinical examination reveals a rather characteristic facial appearance with rounded protuberant cheeks and jaws, giving, in Jones's words, "a cherubic appearance" in the earlier stages. In some cases a little upward turning of the eyes is detectable. There may be some submaxillary lymph gland enlargement. The child is active and of normal intelligence. Both jaws are palpably hard and prominent. The teeth are irregularly placed and some may be missing and the alveolar ridges are wide. The rate of development of the disease varies in different cases, and at a latter age the effects may predominate in the lower jaw. Usually

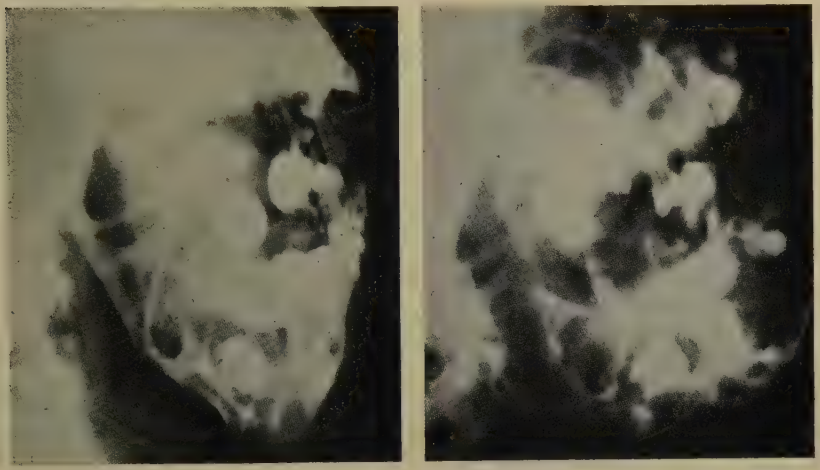

FIG. 519.—RADIOGRAPHS OF THE JAWS OF THE SECOND BOY AT THE AGE OF FOUR, AND AT TEN YEARS.
(By kind permission of Dr. W. A. Jones and the *Brit. J. Radiol.*)

the changes in the jaws are symmetrical and widespread and radiographs show multiple circular cystic areas with heavy bone septa and unerupted teeth may be visible (fig. 518 and 519).

Jones has followed up his series for some years and has observed a tendency to lessening of the facial deformity and a disappearance of the associated lymph gland enlargement. Treatment is confined to orthodontic procedures to straighten erupted teeth.

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Malignant new growths.—Primary malignant new growth of bones are sarcomata or endotheliomata (Ewing's tumour), and are rare under ten years of age, after which they are more frequent. In 119 cases of

sarcoma of the leg and thigh three cases occurred under five years of age, three between five and ten years, and 35 between ten and twenty years, (Butlin and Colby). Primary sarcoma of bone has been seen in infants a few weeks old.

Malignant tumours are not common in children, but the numerical distribution shows a preponderence in bones. In a series of 218 cases of malignant neoplasm in childhood, seventy-nine were osseous in origin. Several factors may contribute to delay in correct diagnosis ; children may be treated for rheumatism, neuritis, sprains or " growing pains " for weeks or months before radiographs are taken ; and no suspicion occur until an actual swelling suggests the true nature.

Symptoms and signs.—Pain is usually a prominent and early symptom and may long precede a visible swelling. Pain, at first transient, later becomes persistent and often worse at night. In the absence of signs of infection such symptoms in an otherwise healthy child should lead to a suspicion of a bone sarcoma. Pain associated with a tumour of large size or rapid growth indicates a malignant process. The absence of pain, however, is quite compatible with the presence of bone neoplasm. Some fever may be present and the blood examination may reveal a leucocytosis.

Location of tumour.—The site of origin may indicate the type of neoplasm. Osteogenic sarcoma usually begins in a metaphyseal region ; endothelioma in the diaphysis ; giant-cell tumours in cancellous bone near an articulation. Exceptions may occur.

Radiography most often affords the earliest and most useful information. Unfortunately few patients are presented for radiographic examination in the really early stages. The good general health and paucity of clinical signs may lead to very dangerous delay. It may be impossible to judge the malignancy of a tumour of bone by clinical examination alone at a stage when operative treatment is of any avail. Team work between clinician, radiologist, and pathologist is essential for best results. Expert radiology is important. Films should be made in two or more planes and stereoscopic views may be necessary for correct interpretation. In the earliest stages the zone of neoplastic tissue shows local increased density and is followed by fine needle-like spicules deviating at right angles to the shaft. Later with extension of the growth along the bone (often with a remarkable limitation at the epiphyseal line) further periosteal changes are seen and eventually osteolysis is revealed. X-ray pictures of the lungs should also be examined for secondary extension even though there be no symptoms or signs in the chest.

Aspiration biopsy from a previously indicated zone is a simple and effective method of obtaining material for microscopy, but great experience is necessary for interpretation of such material. The phosphatase content of the blood may serve as useful evidence. Benign osteochondromas, giant-cell tumours and Ewing's tumour, give normal serum phosphatase readings. The phosphatase is considerably raised in osteogenic sarcoma of the osteo-blastic type and the phosphatase changes afford prompt indication of the effect of radiation therapy. By this means the activity of the primary and secondary growths can be followed. It should be kept

in mind that a zone of benign myositis ossificans, in the immediate neighbourhood of a bone injury, may bear some clinical and radiographic resemblance to osteogenic sarcoma. The American Registry has aided in the simplification of classified bone sarcoma.

Osteogenic sarcoma.—This tumour is commonly related in time to the period of most active skeletal growth. Bone formation is only a potential property of the cells; almost complete reversion to the embryonic state with the production of delicate mesenchymal stroma and a soft fleshy tumour or some differentiation to cartilage or bone takes place. With few exceptions the malignancy is extreme, and even early radical treatment may not avoid a fatal issue.

Periosteal sarcoma. —This is the commonest type. The periosteum is stripped from the cortex and the tumour may infiltrate the bone substance or reach the medulla. Periosteal fibrosarcoma, although producing marked local swelling, may show only a thin line of periosteal new bone at the site of the tumour. The apparent acuteness and other features may lead to erroneous diagnosis of periosteomyelitis.

Medullary sarcoma.—This is probably rare. Sclerosing or ossifying sarcoma is characterized by a large amount of new bone in the tumour. Despite its ivory hard bone content the tumour is very vascular and is of high malignancy. Clinically it grows slowly and may require years to reach considerable size; metastases may appear some years later.

Telangiectatic sarcoma ("Malignant bone aneurism") is intensely vascular, even to appear as mere blood spaces surrounded by malignant tumour cells. It may pulsate. Ready access of cells to the blood-stream creates a grave outlook. The bone shows irregular erosion and spontaneous fracture may be the reason for medical consultation.

Chondrosarcoma may remain amongst the less malignant tumours of bone, but too great a latitude cannot be allowed because rapidly increasing infiltrative and metastitic capacity may arise at any time.

The *treatment* of bone sarcoma in children is often, unfortunately, unfavourable. Results of even early amputation so far recorded are bad. Obviously radiographic examination of the lungs for metastasis should precede any surgical attack. In his summary of evidence on bone tumour Brailsford (1944) says there are indications that radiation therapy administered prior to surgical removal increases the possibility of cure. Coley and Peterson note that osteogenic sarcoma is a radio-resistant lesion and experience in attempting to secure permanent or even lasting regression by X-rays or radium has not been encouraging: nevertheless they favour, in children, a short intensive course of fractional dose radiation before amputation. Radiotherapeutic applications in malignant disease of bones in childhood requires special consideration, and this is discussed by Hilton and Glynn. Amputation should follow promptly after the treatment is completed. Post-operative injection of mixed toxins (Coley) may be given as a possible prophylaxis against pulmonary metastasis.

Endothelioma (Ewing's sarcoma). This is distinctly a disease of childhood: 95 per cent. of a series of 65 cases occurred under the age of twenty-five years (Coley and Peterson). Pain accompanied by gradual

swelling involving a considerable portion of the shaft of a long bone is the usual picture. The upper third of the femoral shaft is a particular site. Periods of increased temperature and some swelling of local lymph glands may be present. Leucocytosis is present. Blood phosphatase is normal. Confusion with a chronic inflammatory lesion may be made and in fact the radiographic appearance may simulate an osteitis of the sub-acute type; the centre of the shaft shows a diffuse rarefaction, an increase in the width of the bone and deposit of new bone parallel to the cortex. Skilful interpretation of the radiographs is highly important in this particular condition. The tumour is radiosensitive and after radiation marked bone production usually takes place in the disease area. The bone sarcoma registry has demonstrated that radiation alone is almost invariably unsuccessful in completely controlling the disease and it should be abandoned as the sole method of treatment for operable cases. This type of neoplasm may give rise to metastases in other bones.

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Secondary malignant new growths.—As compared with adults, children rarely suffer from secondary growths in bone; this is probably because metastases in bone in adults are most often secondary to primary carcinoma of the breast, prostate, thyroid, and malignant hypernephromata, the first three of which are practically unknown in children. In children bony metastases are chiefly due to hypernephroma and renal adeno-sarcoma.

Malignant tumours of the medulla of the adrenal (medulloblastoma) are apt to give rise to bony metastases, especially in the skull bones (fig. 629), thus causing proptosis; and in the ribs; this occurs much more often when the growth is on the left side than when it is on the right (Frew). In the early stages of bony growth there may be pains in the limbs imitating rheumatism. When proptosis appears the condition must be distinguished from (*a*) chloroma by the blood picture; (*b*) infantile scurvy by the absence of other signs and the failure of anti-scorbutic remedies; and from (*c*) the rare condition of plexiform neuroma of the orbit which may occur in children (Parsons). Chloroma, which is so closely connected with leukæmia and multiple myeloma, and which mainly occurs in the flat bones, the ribs, sternum, and skull, is also seen in children.

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DISEASES OF JOINTS

Acute Infective Arthritis

In addition to the forms of acute arthritis specially described in this chapter—pneumococcal, gonococcal, toxic—there are numerous conditions in which acute arthritis may occur. In children the vascularity of the epiphysis favours the advent from the blood-stream of micro-organisms, which in suitable circumstances, such as diminished resistance and injury, may lead to suppuration and eventually infect the joint. Micro-organisms in the blood may also reach the synovial membrane directly, as in adults.

Infection from the throat should be stressed, particularly with regard to arthritis of the knee, in which case removal of the tonsils and adenoids may be important and possibly an essential part of the treatment.

It will be convenient to refer briefly to the ætiology of these forms of acute infective arthritis under two categories: (1) non-suppurative, and (2) suppurative.

(1) **Non-suppurative arthritis,** often transient and mild, may occur after injury and in many diseases. It is often assumed to be rheumatic—for example, when associated with tonsillitis, erythema nodosum, or purpura; but this conclusion is open to considerable doubt. A sub-acute arthritis of the hip, with or without a possible focus of infection in the tonsils or elsewhere, and with a normal X-ray picture, is not uncommon. Since tuberculosis cannot be excluded in these cases at first, treatment is carried out as for this affection. Radiological examination, repeated every few weeks, continues to give a negative result, and the arthritis gradually clears up completely in the course of a few weeks or months, without erosion and without suppuration. These cases are possibly due to a low-grade staphylococcal infection. Butler has suggested the appropriate title of "observation hips" for these cases. Arthritis may appear in connection with mumps, measles, diphtheria, and Vincent's angina, but the extreme rarity strongly suggests that an additional factor such as a mild infection is responsible. Some of these cases may fall in the category of toxic arthritis. Synovitis of the hip-joint during the course of typhoid fever may so stretch the capsule that spontaneous dislocation follows. Of the cases collected by Keen, a high proportion were in children. Although the effusion may become purulent, this does not usually occur. Erosion of the joint surfaces may occur without suppuration. In extremely rare instances acute synovitis has been noted in the course of generalized tuberculosis. Although probable, it has not been proved to be due to miliary tuberculosis of the synovial membrane.

(2) **Suppurative.**—The acute arthritis of infants due to penetration into the joint of a small osteomyelitic abscess near the epiphyseal plate is generally streptococcal or staphylococcal, but may be pneumococcal. It may be excited by injury, foci of micro-organisms latent in the bone being thus activated. The clinical condition is much the same as that of acute infective epiphysitis. Leucocytosis is an important point in diagnosis.

Closely allied are the suppurative joints seen in pyæmic conditions, such as may complicate scarlet fever, otitis media, occasionally in umbilical and cutaneous infections, enteric, and other fevers. In congenital syphilis arthritis may occur in connection with epiphyseal disease, and also independently.

In rare instances micro-organisms belonging to the influenza (Dudgeon and Adams ; Nabarro and Stallman) or coliform groups (Morley Fletcher) have been found in suppurative arthritis. The occurrence of arthritis due to the meningococcus is referred to elsewhere.

Suppurative arthritis may be treated surgically. Chemotherapy must be considered in the light of the bacteriology. Sulphonamide treatment will, of course, be applicable. Penicillin is a valuable therapeutic agent and especially in cases due to gram-positive coccal infection wherein is detected penicillin sensitivity.

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Pneumococcal Arthritis

This is one of the most important forms of infective arthritis in early life, especially in infants. In 100 cases Nitch found that thirty-one were under fourteen years of age, twenty-five of these being less than two years of age. It is much more often unconnected with pneumonia in children, than in adults. Thus, among sixty-nine cases in adults there were nine, or 13 per cent., without pneumonia whereas in thirty-one children under fourteen years there were eighteen cases, or 58 per cent., without pneumonia (Nitch).

In addition to pneumonia, pneumococcal empyema and broncho-pneumonia, the middle ear, pharynx, tonsils, and possibly the conjunctiva, may be portals of entry for pneumococci which eventually reach the joints, and give rise to an arthritis which may appear to be primary. Nattan-Larrier reports arthritis in an infant of three weeks, due to pneumococci derived from a hare-lip operation. Previous injury probably favours infection.

Morbid anatomy. –The exudation into the joints varies in character ; in mild cases there is thick pus of a greenish-yellow colour, whereas in severe cases it is thin and watery. In some instances the effusion is serous. The changes resemble, but are less marked than those in other forms of suppurative arthritis, and except in severe cases the cartilages escape. In a few instances the suppuration has been peri-articular.

Symptoms.—The knee, hip, shoulder, and ankle are the joints most commonly attacked ; one or more joints may be affected. The joint is dis-

tended, hot and extremely painful, but there is no local redness. Opinions differ about the presence of local œdema. Herzog says that it is present, Breason that it is absent, and Nitch that it is present in severe cases only. The swelling may spread widely along the limb. The constitutional disturbance is comparatively slight.

Prognosis was bad in septicæmic and pyæmic cases; it has been thought to be less grave in children than adults. The prognosis may be better in cases with thick pus than in cases with a more watery exudation in the joint. Sulphonamides and penicillin have vastly changed the outlook.

Diagnosis.—The pallor of the skin over the joint is characteristic. The presence of other pneumococcal infections would naturally be of assistance, but acute arthritis occuring shortly after pneumonia may be due to streptococci. In some instances a diagnosis can only be made by bacteriological examination of fluid aspirated from the joint. In suppurative arthritis due to streptococci or staphylococci the constitutional symptoms are more prominent.

Treatment.—Energetic use of sulphonamide therapy, especially sulphathiazole, and sulphadiazine or sulphadimidine may well abort a severe infection and minimize arthritic disease. Surgical treatment may well be considerably modified with the increased use of penicillin in this disease, and especially so where early diagnosis is made.

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Gonococcal Arthritis

Clement Lucas's observation in 1885 that acute arthritis in the new-born might be secondary to gonococcal conjunctivitis attracted little attention in this country until 1899, when he collected twenty-three cases. Gonococcal arthritis in older children as the result of gonococcal vulvo-vaginitis was recognized later.

Ætiology.—In the newly born, gonococcal conjunctivitis is commonly due to direct maternal inoculation at birth. Gonococcal stomatitis and rhinitis may also be contracted at birth and give rise to arthritis. Schiller has collected four examples of the coincidence of this arthritis in infants and their mothers. In forty-four cases occurring in epidemic form in a maternity hospital infection was apparently spread by thermometers used for taking rectal temperatures (Cooperman). In older children, gonococcal ophthalmia may be due to the use of infected towels, sponges, or fingers. Gonococcal vulvo-vaginitis may be caused in the same way, especially in institutions, or by sexual contact with an infected person. Gonococcal urethritis in boys is a much rarer cause of arthritis. Gonococcal arthritis has followed inoculation of the conjunctivæ with gonococci for the cure of

granular lids. In adults gonococcal arthritis is much commoner in males than in females, but in young children this difference is not so marked; in fifty collected cases thirty-three were males and seventeen females.

Morbid anatomy.—The changes vary according to the severity of the attack; in mild cases the inflammation is confined to the synovial membrane; in suppurative cases the cartilages become destroyed and infiltration spreads to the peri-articular tissues. Cooperman describes three forms: (1) the peri-arthritic form, with infiltration of muscles, tendons and ligaments, and flocculent pus between the muscular planes and outside the joint; (2) suppurative arthritis; and (3) non-purulent synovitis.

Clinical picture.—In cases secondary to gonococcal conjunctivitis the arthritis usually appears two to three weeks after the onset of the eye affection. The knee, wrist, and ankle-joints are most commonly affected; according to Lucas, those on the left side are more often attacked, because, as the infant is usually carried on the nurse's left arm, the left side of its body is more exposed to trauma. Other joints, such as the elbow, hip, small joints of the hand, sterno-clavicular, and spine, may be affected, and the tendon sheaths and bursæ may suffer. More than one joint is usually affected. In twenty-six cases described by Emmett Holt the inflammation was confined to one joint in five. The arthritis varies in severity; suppuration may occur, but usually the inflammation is comparatively mild, and ankylosis is extremely rare. Spontaneous dislocation of the hip may result, and from the accompanying change in the head of the femur and in the acetabulum the outlook is poor. In the suppurative form the disease progresses rapidly, the skin becomes red early, and great pain, acute, tenderness, and distension and flexion of the joint are present, with a temperature of 104° F. The milder cases present articular effusion and pain, but no inflammatory redness of the skin. Muscular atrophy occurs early, and is considerable. The disease may last from ten days to eight weeks. Endocarditis is rare. Arthritis and peritonitis have been known to occur together.

Prognosis.—Death is rare, except in marasmic and syphilitic children. As regards complete recovery, the outlook appears to be better than in adults. In cases of gonococcal pyæmia the outlook may be grave.

Diagnosis.—The presence or the history of a recent gonococcal conjunctivitis or vulvo-vaginitis is a very important factor. In older children gonococcal arthritis may imitate acute rheumatism, but salicylates usually fail to influence the disease. Pneumococcal arthritis resembles the gonococcal form in some respects, and, like it, may be polyarticular. Diagnosis may only be possible by microscopical examination of the fluid in the joint. Syphilitic epiphyseal disease may imitate it, but the history and concomitant manifestations should prevent a mistake. Mild cases of gonococcal arthritis may be confused with tuberculous arthritis. In cases of doubt the tuberculin reaction should be tried.

Treatment.—In the first place the primary gonococcal infection of the conjunctiva or vulva should be treated. The pain should be relieved

by salicylates and hot or cold applications ; the joints should be kept at rest and fixed in plaster or other splints. Diathermy is also recommended. In suppurative cases the joint may need surgical treatment but sulphonamide therapy is highly efficacious and penicillin is particularly valuable.

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Acute Arthritis of Toxic Origin

In addition to well-established examples of toxic arthritis, such as gout and that of serum disease, some forms of transient lesions of joints accompanying various erythemas, purpura, and urticaria are, like the cutaneous manifestations, toxic ; similarly joint lesions may occur in Henoch's disease. Schlesinger believes that the interesting condition of intermittent hydrarthrosis, in which attacks of pain and swelling occur so regularly that they can be accurately foretold, is due to angio-neurotic œdema. Further, the synovitis of acute rheumatism is so transient and flits so rapidly from joint to joint without doing any permanent damage that, in the presence of the conflicting reports as to the sterile or infected condition of the joints, it is quite reasonable to regard it as toxic. McClure considers so-called rheumatic arthritis of scarlet fever to be toxic and not infective because the aspirated fluid is sterile. This is open to the fallacy that the causal organisms may have died out or be in the synovial membrane and so not obvious in the fluid. The characters of toxic arthritis are that the manifestations are transient, and that they flit about from joint to joint.

Gout in children is a curiosity, and is a metabolic problem. Garrod mentioned it in two girls of seven and eight years, both with family histories of the disease. Still used to quote a case of gout in a girl aged three and a half years. Cases of supposed gout in sucklings are probably acute infections.

Serum disease.—In hospital practice pain and effusion into the joints are rare after subcutaneous injections of antitoxic serum, but it is commoner in patients who, having had prophylactic doses, are up and about (McClure). The pain is not relieved by salicylates, but it is worth while to give calcium salts after the injection, as recommended by Wright, to prevent the reaction. Tixier and Troisier recorded a case of arthritis during attacks of paroxysmal hæmoglobinuria which they compare with serum disease.

Intermittent hydrarthrosis not uncommonly begins in childhood. In Blanc's case a girl had the first symptoms at the age of seven, and her mother also was affected. Arsenic appears to be the most useful drug (Garrod). Typhoid vaccine was used with success by Miller and Lewin.

Polyarteritis or periarteritis nodosa.—Painful swollen joints may appear, especially in the ankles and knees. Two cases under observation showed peri-articular œdema, nodular swellings, and immobility with considerable joint pains.

Dermato-myositis.—This is associated with some variable joint swelling and flexion fixation, but the pain on attempted movement is principally due to the myositis or myositic fibrosis of the muscle. The patient may be unable fully to extend the elbows, and movements of the hips, knees and feet are painful. Rigidity of the joints, especially at the hip, with limited abduction is detectable. There may be calcium deposition in the region of the great trochanters and around some of the joints (Bailey). (See also p. 1367.)

Pain and some swelling of joints may occur in association with various cutaneous reactions (usually morbiliform or nodular erythema) during or shortly following a course of sulphonamide (especially sulphathiazole) therapy. Similar reactions may appear during the use of barbiturate drugs. Some swellings and limited joint movements may be observed in Henoch's syndrome.

Tuberculous rheumatism.—It is recognized that in the earliest stages of tuberculous invasion, thoracic or abdominal, certain rheumatic pains may occur in the limbs and joints. This may simulate an ordinary form of juvenile rheumatism, but the disease is checked after a short period of rest and no response is obtained to salicylates. It is of importance to suspect this clinical association and a tuberculin test should be made. Occasionally a history of this form of rheumatism may be obtained retrospectively in an established case of tuberculous visceral disease. Sheldon has recently reviewed the general evidence and is able to show quite clearly that rheumatic symptoms may have an important relationship to subsequent serious visceral tuberculosis.

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Arthrogryposis Multiplex Congenita

Synonym.—Amyoplasia congenita (see p. 1376).

Rheumatoid Arthritis

Synonym.—Still's disease.

This condition is characterized, as von Volkmann and A. E. Garrod have insisted, by peri-articular or capsular changes causing fusiform swellings, and by the absence of any primary changes in the cartilages

and bones. The cases correspond to those described as infective arthritis by Goldthwaite and by the Cambridge Committee for the study of special diseases, and are included in their pathological group of proliferative arthritis by Nichols and Richardson. From the atrophic changes in the bones the name "atrophic arthritis" has also been employed. This group includes the cases in children with enlargement of the spleen and lymphatic glands sometimes described as a separate form of joint affection under the name of Still's disease. The reasons for regarding these cases as essentially rheumatoid arthritis are: (1) that the articular changes are the same as in rheumatoid arthritis; (2) that enlargement of the lymphatic glands and of the spleen is not uncommon in adults with rheumatoid arthritis. Thus, from examination of fifty cases, Waterhouse concluded that moderate enlargement of the lymphatic glands is almost constant in the multiple rheumatoid arthritis of young women. The greater prominence of the glandular and splenic enlargement in children is due to the readiness with which the lymphoid tissues react to infection and toxæmia in early life, and not to any specific difference in the disease. Moreover, a case which presented enlarged glands in childhood may in adult life, when the glandular swelling has subsided, be indistinguishable from ordinary rheumatoid arthritis (Garrod); (3) that cases of rheumatoid arthritis in children can be seen (*a*) without any glandular or splenic enlargement, (*b*) with glandular but no splenic enlargement, and (*c*) with enlargement both of the lymphatic glands and of the spleen.

From the category of rheumatoid arthritis are excluded joint diseases due to known micro-organisms, such as the tubercle bacillus, the pneumococcus, gonococcus, streptococci, and staphylococci, the forms of arthritis seen in syphilis and after various fevers, toxic arthritis as in gout and after injections of serum, arthropathies, and the joint changes of hæmophilia.

Ætiology.—In adult life rheumatoid arthritis attacks more females than males, and Diamantberger's thirty-five cases of chronic arthritis in children were made up of twenty-four girls and eleven boys; but in fifty other personally-collected cases there were twenty-six females and twenty-four males. In the study of fifty-six cases, Coss and Boots found a much higher incidence in females (79 per cent.) to males (21 per cent.), this being approximately the same sex distribution as in the adult age groups. The highest incidence, however, occurred between the ages of two and four years. Inheritance does not exert any obvious influence but a familial incidence in rheumatoid arthritis is occasionally striking. The age of onset varies; the disease hardly ever attacks infants under one year, but in a considerable proportion of the sufferers it starts before the end of the third year. In eight out of Still's twelve original cases the disease began within the first three years of life.

Although the exact agent is unknown, it is generally considered that the disease is infective in origin, on the grounds that there may be fever, glandular and splenic enlargement, and in some instances leucocytosis and albuminuria. Stress can hardly be laid on the occurrence of some infective disease prior to the onset in about half the cases, for this is

common in childhood. It has been suggested that it may be a manifestation of attenuated tuberculosis—in fact, a form of the tuberculous pseudo-rheumatism of Poncet (p. 1486), but few cases supply any evidence in favour of this view, and some cases have been proved to be free from tuberculosis. Possibly various micro-organisms of a low grade of virulence may cause the disease, but it is more likely that the cases are all due to one infective agent at present unrecognized.

Morbid anatomy.—There is peri-articular fibrosis with thickening of the capsule and ligaments, and the synovial membrane is vascular and swollen with hypertrophy of its villous processes. In the joints of two severe cases opened during life the synovial membrane is described by Whitman as replaced by soft red granulation tissue. The cartilages are normal or present some pitting at the margins where overlapped by the enlarged synovial fringes. There is an absence of osteophytic outgrowths and of the fibrillation and erosion of the central parts of the cartilages characteristic of osteo-arthritis. There may be adhesions in joints severely affected. The adjacent bone shows rarefaction. Osteoporosis may eventually become marked and some osseous deformity appear. The pelvis may show a diminished antero-posterior diameter. The enlarged lymphatic glands show chronic hyperplasia. The glands in the portal fissure may be enlarged. Pericardial and pleural adhesions may be present. Amyloid disease of the spleen, liver, and other organs has been reported (Herringham, Whitman).

Clinical features.—The onset is usually acute and febrile ; in some cases it is described as gradual. The course of the disease is prolonged. Exacerbations of arthritis with fever, especially at night, and sweating, are not uncommon. In other instances the temperature is almost continually raised to 100° to 101° F. Tachycardia is always present in the active phases of the disease.

The joints usually affected are the knees, wrist, ankles, interphalangeal, especially of the hand, the metacarpo-phalangeal, and the cervical spine ; the temporo-maxillary and sterno-clavicular are not attacked so frequently as in adults. In some instances the larger articulations, *e.g.* knees, suffer to the relative exclusion of the smaller. The joints are symmetrically affected, and present, especially those of the hand, a characteristic fusiform appearance which is mainly due to peri-articular fibrosis and œdema, for there is little effusion into the joint cavities. Torticollis from affection of the cervical spinal joints may occur as an early manifestation. A degree of cervical dislocation may appear. Radiography shows osteoporotic transparency of the bones and absence of osteophytes. On movement, which is always limited, crackling may be felt, but there is no bony grating. The joints are comparatively free from pain and tenderness but pain is caused by passive movement (fig. 520–522).

Muscular wasting is prominent and contractures, particularly of the larger joints, are common. Clubbing of the fingers has been observed.

There is no liability to endocarditis, but a hæmic murmur may appear. As the disease advances the pulse becomes rapid. Enlargement of the

FIG. 520.—RHEUMATOID ARTHRITIS WITH SWELLING OF PHALANGEAL AND CARPAL JOINTS.

FIG. 521.—RHEUMATOID ARTHRITIS: EARLY ACUTE STAGE.

Note the swelling in the knee-joints and ankle-joints, and the œdema of the feet.

FIG. 522.—RHEUMATOID ARTHRITIS: CHRONIC WASTED STAGE.

lymphatic glands is specially seen in young children. The enlarged glands are chiefly related to the affected joints, but the change may be general. The glands increase in size during the febrile periods when the joint changes are progressing, and subside in the intervals. They may reach a considerable size, but never suppurate and the skin over them is natural. Enlargement of the spleen, which is quite moderate, is also more prominent the younger the patient, and is an early sign which may disappear. The liver may also be increased in size, and this also may disappear as the acute stage of the disease subsides. Albuminuria and casts occur in a few cases ; albuminuria may be constant, or only appear during the febrile exacerbations.

In a collection of fifty published cases of rheumatoid arthritis in children, many of which were probably recorded on account of visceral manifestations, enlargement was noted of the glands in thirty-nine, of the spleen in twenty-eight, of the liver in eight, and six had albuminuria.

The children are thin, and often show arrest of development. There is usually some hypochromic anæmia, and leucocytosis has been noted during febrile exacerbations. The Wassermann reaction is negative. The skin is pale and usually very smooth. The face has often a waxy pallor with a malar flush, and pigmentation is occasionally noticed. Slight exophthalmos is not uncommon. In a few instances jaundice has been present, and some grave cases have had purpura. Sweating may be prominent although fever is absent. The erythrocyte sedimentation rate is raised. Occasionally, acute rheumatism and rheumatoid arthritis exist at the same time or at different ages in the same child. A young adult may develop acute rheumatoid arthritis and objective examination reveal initial disease of many years standing. Cardiac signs, including endocardial and pericardial, and nodules may definitely indicate concurrent rheumatic disease in rheumatoid arthritis (Field). Acute pericarditis, pleurisy or high pyrexia may shortly precede the onset of enlarged lymph glands and the typical joint changes (Schlesinger). The two diseases are usually regarded as separate entities but pericardial adhesions (usually undetectable clinically) were noted by Still in some cases. Some regard the two diseases as intimately related and Charcot considered " the two different manifestations of one and the same diathetic state." After a careful study of the morbid anatomy, Langley considers that Still's disease is an independent condition.

Prognosis is probably better than is usually believed, and recovery may certainly occur. Visceral enlargement is an early sign, often disappears, and is not necessarily bad prognostically. Improvement was noticed by Still after intercurrent attacks of measles, scarlet fever, and jaundice. A fluctuating and phasic variation in the activity of the disease is apparent. Muscular wasting and contractures may proceed to a severe grade. The disease appears to have a life history of months, or perhaps a few years, after which the general constitutional condition improves, tissues and muscles regain a more normal contour, appetite and a good colour return. Ultimate complete recovery may be achieved.

Prolonged rest and avoidance of injury to the actively affected joints will usually enable recovery without any bony ankylosis.

Diagnosis.—In the acute phases the disease must be distinguished from rheumatic fever by the failure to react to salicylates and by the more marked articular changes. Diagnosis from other low-grade infections of a large joint may be impossible until other joints have become involved. Later it must be differentiated from other forms of chronic arthritis. There is a rare condition of chronic peri-articular fibrosis with rheumatic nodules, which may follow acute rheumatism, Jaccoud's chronic fibrous rheumatism. The rigidity of the spine may suggest caries, and the joint changes and splenic enlargement be erroneously regarded as rickety.

Treatment.—A long and fluctuating illness must be envisaged and the parents should be so informed in order to gain co-operation and patience. The environment should be favourable, warm and dry, and the child kept as cheerful as possible. Anxiety and fear certainly aggravate the disease. The nutrition must be kept to as high a level as possible. Periods of anorexia may be troublesome. A full varied diet is to be encouraged. The vitamin supply must be adequate and in the case of vitamins D and C liberal quantities should be given. Some recent observations have been made in cases treated with high but subtoxic doses of vitamin D_2, *e.g.* 200,000 units daily for several weeks, and favourable results have been obtained (Ford). Boland finds no support for the idea that rheumatoid arthritis is ætiologically related to hæmolytic streptococcal or other penicillin sensitive organisms, and he observed no improvement following one and a half to three and a half million units of penicillin. Iron should be given also. Small fresh blood transfusions may be a useful procedure. Medicinal acid with meals is helpful especially when hypo- or achlorohydria is present. Suitable bed cradles and light limb splinting must be considered in the individual cases. The tendency for knee contracture must be specially observed, and light plaster dorsiflexion splints may be necessary to rest the wrists and hands periodically and to prevent undue use of the affected joints or to check any tendency to palmar flexion and ulnar deviation of the hands. Wool protection may be helpful to the elbows and ankles. Cervical arthritis may need a period of special immobilization especially to avoid or correct a dislocating deformity.

Septic foci must receive adequate attention at suitable times, although some temporary accentuation of the active signs of the disease may be expected following tonsillectomy or septic dental extraction. Occasionally very dramatic improvement follows removal of infected tonsils. Various special measures may be considered according to the age and medical status of the child—passive hyperæmia to the limbs may be tried; occasionally protein shock—induced by T.A.B. vaccine, or by sterile milk injection (in a series of half to one, two or five c.cm. at three-day intervals) is of value but cannot be relied upon. Physiotherapy, apart from light massage to muscles, should be postponed until the general condition is improved. Natural sunlight or ultra-violet radiation has a favourable effect. Short-wave diathermy may have comforting effects

on specially painful joints; or light kaolin poultices may be applied for a similar purpose. Sleep might be aided by aspirin-codeine powders, but fortunately pain is usually minimal in the juvenile disease. Opinion varies as to the value of gold treatment. After a period of general treatment and providing the nutritional state is fair, it is safe to give, say, myocrisin, 0·005 to 0·01 gramme at weekly intervals for six doses and possibly repeated at a later date; the usual control observations should be made on the leucocytes and sedimentation rate, and upon the urine.

In the improved and ambulant stages of the disease the child must avoid undue stress and strain upon joint structures; stretching of unrecovered peri-articular tissues may lead to late deformity or further activation of inflammation. Ambulatory treatment, however, should be insisted upon whenever possible, in order to avoid unnecessary stiffness.

In some severe intractable cases splenectomy has been recommended. On this, the reader is referred to the papers by Bach. The possibility that "rheumatoid disease" may be related to pituitary-adrenocortical disturbances has raised the question of the value of ACTH and cortisone in treatment. This is at present in the experimental stages and is discussed by Schlesinger and Cathie.

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Osteo-Arthritis

This form of joint disease, characterized by primary changes in the cartilages, lipping and eburnation of the articular surfaces, and osteophytic formations is extremely rare in children. A familial form, possibly a distinct disease, has been described (Armstrong). It appears to be rather the late result of some destructive change in the joints such as that induced by hæmophilia or inherited syphilis, than comparable to the osteo-arthritis of more advanced life. Congenital syphilis may cause multiple osteo-arthritis with Heberden's nodes which is not necessarily progressive. Eye changes such as keratitis and choroiditis are apt to be associated with this form; out of four cases of this kind recorded by Still three had interstitial keratitis. Although apparently occurring in syphilitic subjects, the condition is not benefited by mercury and iodides, and in this respect resembles Charcot's arthropathy. It has been known

to affect several joints and thus to simulate rheumatoid arthritis. Until the changes in the joints are sufficiently advanced to show in X-ray pictures it may be difficult or impossible to distinguish between the two diseases. It may occur as a sequel in osteo-chrondritis.

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Syphilitic Arthritis

The following forms of arthritis may occur in congenital syphilis :

(1) In young infants *syphilitic arthritis* is rare, but it may complicate syphilitic epiphyseal disease. Suppuration in connection with syphilitic epiphysitis may extend into the joint, and occurrence of this suppuration is generally assumed to be due to secondary streptococcal or staphylococcal invasion, but the pus has been found to be sterile (Marfan). This form of suppurative arthritis, which is seldom seen after six months of age, may or may not be confined to one joint. Excess of synovial fluid in a joint is not uncommon in connection with syphilitic epiphysitis.

(2) A form of arthritis deformans with bony changes as in osteo-arthritis (*Charcot's arthropathy*).

(3) *Chronic effusion*, nearly always into the knee-joints, and usually bilateral, though one knee may be more swollen than the other. This form, first recognized by Clutton, occurs between the ages of six and fifteen years. It is specially related to the occurrence of interstitial keratitis, and it has been estimated that 75 per cent. of the cases show this eye change (Dunlop), which usually appears after the synovial effusion. The sexes are equally affected, thus differing from interstitial keratitis which is more frequent in girls.

Other forms have been described, but they are excessively rare. Knowledge of the pathological changes is imperfect. In some instances there has been little or no morbid lesion, in others hyperæmia and thickening of the capsule or small gummata or gummatous infiltration of the synovial fringes have been described.

Syphilitic arthritis is usually associated with sclerosis of the neighbouring bone. Some erosion may occur with irregular sclerosis of the bone in the metaphyseal area.

Clinical picture.—The effusion comes on insidiously with little or no pain, and, unless treated, runs a chronic course. The knees are affected in a high percentage of the cases ; von Hippel found this in forty-one out of his forty-three cases, and in thirty-five of the cases the knees were the only joints attacked. The mobility of the joints is little interfered with, and local redness and heat are absent. Usually there is no bony enlargement, but some cases present thickening of the synovial membrane. The condition is probably often mistakenly regarded as tuberculous, and it has been suggested that this is responsible for the long course of such cases.

If treated with mercury and iodides, they usually clear up in about two

months, whereas splints and rest do not effect any improvement. When specific treatment is imperfectly carried out a relapse may occur. In rare instances, however, tuberculosis appears to supervene in a joint primarily syphilitic. This complication may explain why some cases do not respond to specific treatment.

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JOINT AFFECTIONS IN NERVOUS DISEASES

Joint affections occurring in connection with nervous diseases may be thus divided.

(*a*) *Associated with acute diseases of the nervous system.*—In rare instances acute poliomyelitis is accompanied by arthritis in the paralysed extremity. Poynton discussed this condition and pointed out that, at least in some outbreaks of poliomyelitis, arthritis is apparently common and that this may not be generally recognized. One joint only, such as the ankle, may be affected either synchronously with the onset of the paralysis or some weeks later. In another form the small joints of the hand suffer; Coutts described this form in a brother and sister. It is open to discussion whether or not the joint affection is due to an ultra-microscopic organism responsible for acute poliomyelitis or to some other infection of the less resistant joints of the affected extremity. From the presence of pain and loss of power acute rheumatism is likely to be diagnosed, but salicylates fail to relieve the symptoms. Infantile scurvy in an early stage may also imitate poliomyelitis with arthritic manifestations.

In epidemic cerebro-spinal meningitis there is, occasionally, intra- or extra-articular suppuration due to the meningococcus. Usually meningococcal arthritis subsides without injuring the joint, and may be hardly noticeable, but sometimes it is a prominent feature. It may be associated with the chronic (posterior basic) form of meningococcal meningitis. In some instances, of which Cecil and Soper have collected five, meningococcal septicæmia is not accompanied by meningitis; it is therefore possible that meningococcal arthritis may occur independently of meningitis, in meningococcæmia.

(*b*) *Associated with chronic nervous diseases.*—Syringomelia rarely occurs in childhood, but the occurrence of arthropathies of the Morvan type has been recorded in children (Clarke and Groves, Fletcher).

Hysterical joints in children are usually seen in girls approaching puberty. The affected joint, commonly the hip, sometimes the knee, which is free from any swelling, or bony change when examined by X-ray, is rigidly fixed by muscular contraction, and is intensely painful until the patient's attention is distracted. In the foot, varus is the usual direction of the deformity. There may be evidence of definite neurosis and of cutaneous hyperasthesia or anæsthesia. The diagnosis from early tuberculous arthritic disease must be made with great care.

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HÆMOPHILIC JOINTS

Arthritic manifestations are extremely common in hæmophilia and contrast with the great rarity of hæmorrhages into other serous membranes.

Ætiology.—The liability to these articular manifestations is most prominent in early life, the first attack commonly occurring between the fourth and seventh years, and diminishes with advancing years. The joints suddenly swell as the result of strain or injury, which may be so slight that the onset is described as spontaneous. The attacks, which may closely resemble ordinary synovitis, are more easily induced at one time than another. The disease affects males almost invariably and is commonly hereditary, being transmitted, as a rule, through the females.

Morbid anatomy.—That hæmorrhage occurs into the joints is proved by aspiration during life and by examinations of hæmophilic joints after death. König described three stages—hæmorrhage (hæmarthrosis), inflammation, and deformity. After repeated attacks the synovial membrane presents fringes with a seaweed appearance of a rusty colour, due to altered blood pigment; there are adhesions, the cartilages degenerate, and eventually the changes seen in osteo-arthritis result. Wright suggests on the analogy of the superficial "serous hæmorrhages," that the fluid in the joints is often serous, and not hæmorrhagic.

Clinical picture.—The knee is most often attacked, in about half the cases; then the elbow, in about a quarter of the cases; and the ankle and other joints, including those of the fingers. Several articulations may be affected in the same patient. Three stages have been described. At the onset the joint becomes distended and painful, but not particularly tender, and the skin over it is stretched, but not red, although it may be slightly warm. The effusion is soon absorbed, and the joint appears little damaged. In the second stage a form of chronic arthritis has resulted from repeated attacks, and thickening of the synovial membrane and some passive effusion are present. Splinting may be required for a year or even two before the local signs subside. In the third stage the joints become permanently deformed and partially ankylosed. X-ray examination reveals in the early stages an increase in the joint space; later areas of cancellous destruction appear in the subarticular bone, and degrees of local osteoporosis occur. Erosion of joint surfaces and cartilage destruction follows and the joint takes on the appearances of severe secondary osteo-arthritis. Epiphyseal ossification may be disturbed.

Prognosis.—The vast majority of "bleeders" eventually suffer from some arthritic crippling, but the liability to hæmarthrosis diminishes as age advances, and the prognosis therefore improves as time goes on.

Diagnosis.—In a known "bleeder" any joint affection should be suspected to be of this nature, and surgical interference as a rule forbidden. An urgent operation, *e.g.* for appendicitis or even for removal of tonsils, can be carried out more safely, if preceded immediately by blood transfusion, preferably from the father. Unfortunately hæmophilics sometimes conceal their diathesis, and the disease may be regarded as tuberculous, rheumatoid arthritis, or even osteomyelitis. In recent attacks of obscure arthritic swelling in boys the possibility of hæmophilia should be considered, and inquiry made on this point before active measures are adopted. As hæmophilic joints are particularly likely to be regarded as tuberculous, a tuberculin patch test, which does not involve puncture or incision of the skin, may be employed in a doubtful case.

Treatment.—The joint should be kept at rest, if necessary by splints, and soothing applications or an ice-bag applied. The general treatment of hæmophilia should of course be carried out.

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CLUBBING OF THE FINGERS

Synonym.—Hippocratic fingers.

Definition.—A swollen condition of the terminal phalanges, with curving of the nails of the fingers and toes; it is almost always symmetrical, and is due to changes in the soft parts.

Ætiology.—It is most commonly due to intra-thoracic conditions of an infective nature, such as bronchiectasis, emphysema, chronic pneumonia, fœtid bronchitis, and chronic pulmonary tuberculosis. It is seen in congenital heart disease, especially pulmonary stenosis with cyanosis, and may then be associated with an analogous change in the nose and ears. It is also occasionally present in a slight degree in advanced valvular disease due to rheumatic endocarditis, and usually appears in some degree, in subacute infective endocarditis.

It always accompanies osteo-arthropathy. Clubbing of the fingers is not uncommon in hypertrophic biliary cirrhosis of the liver with chronic jaundice. It is more often seen in this disease in children than in adults. It may also be associated with chronic jaundice due to other causes. In rare instances it has been observed in sarcoma and hydatid of the lung, lymphadenoma of the mediastinum, amyloid liver, congenital dilation of the colon (J. Thomson), rheumatoid arthritis, enterogenous cyanosis (Stockvis, V. de Borgh), ulcerative colitis, pyelonephritis (Marfan) and chronic steatorrhœa. Exceptionally the condition has been said to be congenital. It has also been seen in delicate children with defective circulation, but without any evidence of definite disease (Thomson and

Sheldon) and it has been noted in perfectly healthy individuals, and then to be familial (F. P. Weber).

Pathogenesis.—The factors most probably concerned are: (*a*) The local action of toxins formed elsewhere on the soft tissues of the nail bed, or (*b*) the mechanical stagnation of blood in the nail bed due to circulatory disturbances such as would result from failure of the right

FIG. 523.—CLUBBING OF FINGERS IN A BOY AGED TWELVE YEARS.
(From a photograph supplied by the late Professor L. Findlay.)

FIG. 524.—SKIAGRAM OF FIG. 523.
(Supplied by the late Professor L. Findlay.)

side of the heart, or (*c*) a combination of (*a*) and (*b*). Thus, it has been suggested that cyanosis –for example, that due to congenital heart disease induces toxæmia by interfering with the excretion of poisons by the lungs. The question of the causation cannot be considered as settled, for many cases, in which the conditions suitable for the production of clubbing are present, do not show this change. It has been suggested that the condition is due to trophic impulses conveyed through the nervous system ; but, except that neuritis and clubbing of the fingers are in rare cases associated, there is no evidence of this.

Morbid anatomy. There is no change in the bones, and the nature of the alteration of the soft tissues has been variously described. In favour of the view that the swelling of the soft parts is due to vascular engorgement and œdema, it has been stated that the bulbosity can be removed by pressure, and that it disappears in fingers preserved in spirit. Hyperplasia of the soft tissues, enlargement of the papillæ of the dermis, and increased quantity of fat (Emerson), have also been described.

Clinical aspect.—Clubbing of the fingers usually comes on gradually, but it has been noticed within two weeks from the onset of the causal disease (West). The fingers are more often and more rapidly affected than the toes ; usually all the fingers share in the change, but sometimes the index finger and thumb are chiefly affected and in rare instances the clubbing is confined to one or two fingers. The terminal segments are much enlarged, and their tips are cyanotic. The nails are curved longitudinally and transversely, are often longitudinally striated, and may be unduly brittle (fig. 523 and 524). Their growth is more rapid than in health, and they are also peculiar in that the root of the nail is raised and unusually movable. The ends of the fingers have been compared to the bowl of a spoon, to a drumstick, and when seen in profile, to a parrot's beak. The bulbous fingers are usually free from pain, and there is not any alteration in sensation. When the cause of the condition—for example, an empyema—is removed the clubbing disappears. Clubbing may be asymmetrical. The *treatment* is that of the associated disease.

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HYPERTROPHIC OSTEO-ARTHROPATHY

Synonym.—Hypertrophic pulmonary osteo-arthropathy.

Definition.—Symmetrical enlargement of the hands and feet, with clubbing of the fingers and toes, periostitic-like thickening of the long bones, especially in the neighbourhood of the joints, and articular inflam-

mation. It is a secondary manifestation of morbid processes elsewhere, usually in the lungs.

Ætiology.—It is about five times more frequent in males than in females, whether children or adults. P. Marie, who described the condition in 1890, considered that it was always secondary to disease of the lungs, and due to toxins absorbed from lesions in these organs; he therefore called it "hypertrophic pulmonary osteo-arthropathy." Although it is now recognized that it may occur in cases in which the lungs are healthy, Marie's statement holds good in the majority of cases. The intra-thoracic conditions with which it is associated are bronchiectasis, chronic pneumonia, chronic pulmonary tuberculosis, empyema, and malignant disease of the mediastinum or lung. In rare instances it has been noted in hypertrophic biliary (Hanot's) cirrhosis, and still more rarely in tuberculous disease of the spine, and intra-thoracic lymphadenoma. It may occur with sarcoma of a bone, and this before there are any signs of secondary growths in the thorax. The changes may appear in subacute form as in a recently observed case in which there was a primary sarcoma of the pharynx and which improved after radiotherapy, but some months later, secondary tumours appeared radiologically in the lungs at which time typical hypertrophic arthropathic changes made their appearances. A patient with an infected thoracic dermoid cyst developed the arthropathy. In some cases the cause has not been apparent.

Pathogenesis.—It was thought by Marie that the peri-osteo-arthritic changes were due to toxins absorbed from the lungs, and Bamberger (1889), who described the condition before Marie, though less fully, considered that its onset was specially related to the sputum becoming fœtid. This explains to some extent why bronchiectasis and pulmonary tuberculosis may be present for years without any associated osteo-arthropathy. In 1896 Thorborn and Westmacott put forward the view that the changes were due to tuberculosis, and Poncet and his followers regard it as a form of tuberculous pseudo-rheumatism—namely, due to toxins produced in tuberculous foci elsewhere. Compere and Adams as a result of experimental investigation express opinion that the changes of osteo-arthropathy are not due to toxin but can be explained on the mechanical basis of blood stasis, or of poor aeration of the blood, creating changes in the acid base equilibrium. Infection and suppuration are not essential to the production of osteo-arthropathy.

Morbid anatomy.—There is a deposit of new periosteal bone on the shafts of the long bones, especially the lower ends of the radius, ulna, metacarpals, and first two rows of phalanges; less often the lower ends of the humeri, the upper extremities of the radius and ulna, and the bones of the lower extremities, particularly the tibia and fibula near the ankle-joint, are affected. The shafts may show a diffuse sheath of periostitic bone, but the sheath is thicker near the joints. In some instances this change is seen in other parts of the skeleton. These changes are symmetrical on two sides of the body. The joints usually contain fluid, and may show definite evidence of inflammation, such as gelatinous thickening of the synovial membrane. There is no bony change in the terminal

phalanges, which are in the same condition as in clubbed fingers. The ductless glands are normal. The newly-formed bone is friable, and, like that of ordinary periostitis, is composed of layers parallel to the long axis of the bone. This chronic proliferative osteitis may form a shell of new cancellous bone one to five mm. thick, completely surrounding the tibia, fibula, radius and ulna. Rarefaction of the underlying shaft has been described as a distinguishing feature from ordinary osteoperiostitis. Microscopically there is no evidence of tuberculosis.

Symptoms.—Clubbing of the fingers is always present, and in addition there is enlargement of the ends of the bones and prominence of joints, especially the wrists and ankles, and sometimes the knees, elbows and phalangeal joints. The bony thickening and irregularity may be felt, and the enlargement of the ends of the bones is exaggerated by the swelling of the overlying subcutaneous tissues and by the atrophy of the muscles of the limbs. Thickening of the soft tissues around the joints—especially wrists, elbows, ankles and knee—may be considerable and in fact be responsible for most of the palpable swelling. Also some swelling may appear round the eyes and the general facial appearance be that of a "tired expression" with some suffusion and œdema of the conjunctiva. The joints may be tender, often contain fluid, and their movements are clumsy and somewhat impaired. The course of the disease varies; acute and chronic cases have been described, and not uncommonly there are distinct exacerbations, during which the articulations become painful and swollen, the skin over them red, and the temperature of the body somewhat raised. Excessive perspiration is common. Kyphosis in the dorsi-lumbar region may occur, but is due to pulmonary or other lesions. When the causal condition, such as empyema, is cured, the bone lesions undergo slow resolution.

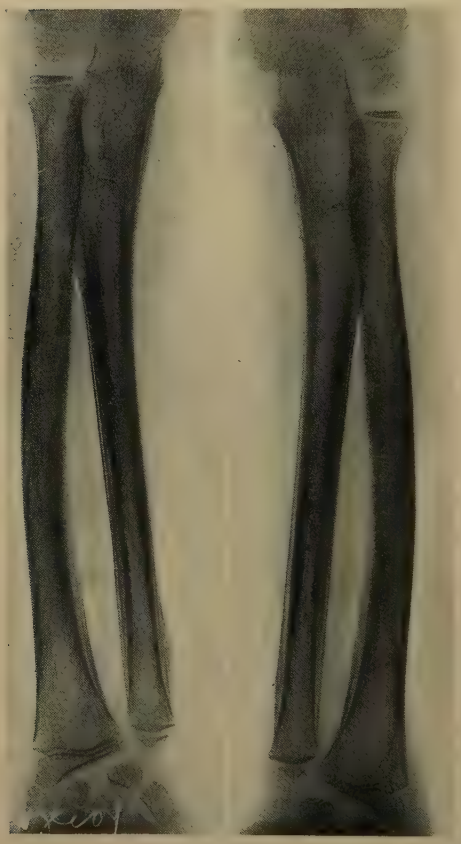

FIG. 525.—PULMONARY OSTEO-ARTHROPATHY.

Linear periosteal thickening in pulmonary osteo-arthropathy in a child with severe bronchiectasis.

Diagnosis.—Acromegaly is unknown before puberty; it is

characterized by elongation of the face and prognathism and is not accompanied by clubbing of the fingers. From rheumatoid arthritis X-ray examination will at once distinguish it.

Treatment.—It is essential to treat the underlying cause : if successful the secondary effects included under the title of this section may clear up, either partially or completely. Pain is not often troublesome, but if so relief may be obtained from hot applications or salicylate.

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SEPARATION OF EPIPHYSES

This may occur at any time until the epiphysis unites. It is more usual at an age when only an intervening cartilaginous disc is present. The separation is between the disc and the shaft ; the younger the patient the cleaner the line of separation. Often a fragment of the diaphysis is carried with the displaced epiphysis. The periosteum is easily stripped from the shaft, but firmly adheres to the epiphysis. Untreated new bone develops under the stripped diaphyseal periosteum and impairs linear reduction. Remodelling, however, will occur. Even slight persistent displacement of the lower radial epiphysis will interfere with radio-ulnar movement. Similarly, displacement of the upper femoral epiphysis is important ; disabling coxa vara may result. Immediate and accurate epiphyseal replacement is very important and should be carried out by a surgeon and controlled by X-ray examination. Open operation may be necessary properly to reduce a difficult separation. As a result of the mishap the bone may grow more slowly than its fellow.

Separated epiphysis can usually be recognized by the signs of fracture without crepitus. In older children a slight grating may be elicited.

The upper end of the humerus.—Epiphyseal separation is usually seen after the age of seven years, and after indirect violence. The displacement is variable in degree and in direction and rarely complete because the cup shape is somewhat protective. X-ray diagnosis is essential.

Lower end of the humerus.—Epiphyseal displacement is more commonly combined with fracture and is usually due to a fall on the elbow. Forward displacement of the upper fragment may cause danger by pressure on the brachial artery or median nerve. A tense fusiform swelling appears within a few hours. This particular injury is serious and after exact radiological diagnosis it should be placed in the care of the expert, who may find the task of adequate reduction and maintenance of apposition no easy matter. Displacement of the internal epicondyle may cause some temporary ulnar neuritis, or ulnar neuritis may be more gradual in onset and persistent and so require anterior reposition of the nerve.

Lower end of radius.—The deformity is similiar to, but somewhat less obvious than, that seen in ordinary Colles's fracture. Accurate and completely satisfactory treatment is essential in order to avoid possible loss of normal growth of the radius with subsequent important deformity.

Similar argument applies in separation of the *lower tibial epiphysis.*

Hyperextension of the knee may cause the *lower femoral epiphysis* to move forward thus producing obvious acute deformity.

Upper end of femur.—The common age of occurrence is eleven to fifteen years, and the separation may be sudden from gross injury or develop slowly as a static deformity following injury, especially in an obese child. The former is clinically the same as an intracapsular fracture. In the latter a limp appears and the hip becomes painful due to the deranged angle of the femoral neck, interfering with normal mechanics in the acetabulum ; the clinical and radiological signs of coxa vara of the epiphyseal type are determined (p. 1523).

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FRACTURES

Fracture in normal bones is of course common in children, but owing to the softness of the bones and the thickness of the periosteum, partial or incomplete subperiosteal fracture is frequent. This may make immediate diagnosis not easy, especially in the clavicle or forearm or tibia. A variable degree of pain, some immobility and local tenderness may be the only evidence. These fractures may be thought to be early osteomyelitis. Deformity may be absent ; a week or so later callus formation makes the diagnosis evident. Greenstick fracture is a common form, giving rise to deformity without crepitus ; angulation may be considerable when both forearm bones are so fractured. Healing occurs well in childhood fracture and even large amounts of callus are finally absorbed leaving the bone in a practically perfect condition. Treatment therefore should be of such a high standard that no shortening and no deformity result so that further natural bone development is unimpaired. Fracture may occur from minimal trauma in some conditions, *e.g.* rickets, cœliac disease, osteitis fibrosa, fibrous dysplasia, osteosclerosis fragilis, bone cyst ; and special considerations in the treatment are needed.

Birth fractures.—These unite quite well. Natural re-adjustment is remarkable. Also there is apparently a surprising absence of infantile discomfort even in an angular femoral fracture. Simple immobilization of the affected limb with bandage for two or three weeks, after which free movement can be allowed, is quite safe. Massive callus is not unusual but it disappears in a few months. Fractures in association with osteogenesis imperfecta will be self-evident on clinical and radiographic examination. Undue traction on the legs and arms during breech delivery may cause periosteal injury in the neighbourhood of the

proximal epiphyses of the humerus and femur; this may be shown radiographically fourteen days after birth as an ossifying periostitis. Recovery is spontaneous. The swelling and tenderness and limited movement simulates a birth fracture (Snedecor).

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OSTEOMYELITIS

Acute osteomyelitis.—Whereas sepsis in a bone can arise from direct extension of infection from local sources this is essentially an acute pyogenic infection of the metaphyseal section of the shaft of the long bone arising from blood-borne bacteria. The disease may remain in the epiphyses, but this is undoubtedly extremely rare. Staphylococcus aureus is the organism in most cases; other types of staphylococci, streptococci, and pneumococci are occasionally found. The origin of the infection may be occult, or abrasions, boils, septic teeth or upper respiratory sepsis may be evident. Local injury such as a blow, strain, or even a slight fall may shortly precede the onset. In some cases the disease appears initially as a bacteræmia or septicæmia, and the micro-organisms then settle in favourable situations. Probably a small traumatic hæmorrhage favours the localization. Some strains of staphylococci may have a special affinity for osseous tissue. In severe cases multiple bone infection with persistent septicæmia and later pyæmia takes place. The processes of inflammation are rapid; hyperæmia, œdema, and pus formation occurring in quick succession, so that considerable tension soon develops. The infection spreads along the Haversian canals to the surface, causing subperiosteal effusion, down the medullary canal, or rarely through the epiphysis. The periosteum is raised off the bone surface, but owing to its close attachment to the circumference at the epiphyseal plate, infection does not usually spread into the neighbouring joint unless the metaphysis is intra-articular, *e.g.* the hip. Wide elevation of the periosteum causes impairment of blood supply to the cortex and bone necrosis results which later may form sequestra. The deeper osteogenetic layer of the separated periosteum produces a new covering of bone which becomes the involucrum and in which cloacæ remain for the escape of deep pus and small sequestra. Larger sequestra cause persistent suppuration. The disease is common and potentially or actually serious and is more common in boys. The lower end of the femur and upper end of the tibia are the most frequent sites. However, any diaphysis is vulnerable to this disease including the ilium and the vertebræ.

Symptoms and signs.—Varying with the degree of general infection initial toxæmia may be profound or slight. The degree of fever, possibly rigors, delirium, headache and dryness of the mouth are some guide. In the case of a long bone, pain is indicated near one or other end, although joint movement and muscular tone may be quite unaltered. Local and considerable tenderness in the metaphyseal region of the

suspected bone is the major physical sign, especially in early cases. Leucocytosis occurs rapidly. Later, the signs are intensified by the development of pus in the subperiosteal site and extension of acute disease along the bone to the shaft; thus heat, œdema, and fluctuation may be detected. If the early clinical picture and its pathology is kept in mind dangerous procrastination in diagnosis will be avoided. In this respect a most careful check against an unfortunate tendency to label the condition rheumatism must be made. Acute articular rheumatism limited to one joint is very rare and in acute osteomyelitis the tenderness is osseous, not articular, even though in some cases a small joint effusion is detectable. In this dangerous bone disease it is bad treatment to "try salicylates." Occasionally severe pain in a limb may occur in early acute poliomyelitis or even in scurvy, but the associated picture clarifies any doubt in diagnosis. Fortunately the commonest sites, lower femur and upper tibia, lend themselves to early recognition by virtue of the superficial position of the bones. However, the loose attachment of the periosteum at the distal part of the femur favours early abscess formation and bone sequestration. The disease of the upper end of the femur may yield a difficult clinical picture with severe constitutional features and in early childhood the hip-joint is often involved.

Osteomyelitis of the pelvic bones is associated with profound toxæmic signs and the local features of the disease may be over-shadowed. Intra-pelvic or subgluteal abscess develops or in the case of pubo-ischial location of the osteomyelitis an abscess may track towards the bladder.

Osteomyelitis of the vertebræ is fortunately rare. If it arises in the vertebral body diagnosis is difficult. Severe pain in the back, often radiating along irritated nerve trunks, is conspicuous. Abdominal pain is sometimes the first symptom, spinal rigidity occurs and the patient may loudly resist attempt at movement. Extension of the suppuration may occur into the posterior mediastinum: mediastinal abscess may extend to the left and to the right of the vertebral column and complete drainage may eventually require bilateral posterior mediastinotomy (Neuhof). Suppuration may extend into the lumbar region or down the psoas probably more commonly than into the posterior mediastinum. Fairbank has seen a typical abscess shadow, such as is commonly seen in the dorsi-lumbar region on either side in spinal caries, in a case that was undoubtedly not due to tuberculosis since there was an acute onset, with marked leucocytosis; surprisingly the abscess slowly disappeared and the child got quite well without the abscess ever having been opened either by nature or by the surgeon. More fortunately the disease may attack the spinous process or lamina and so local signs are more evident and pus usually tracks to the surface easily; but occasionally an acute epidural spinal abscess is formed and causes rapid compression of the spinal cord. The dura, however, is more usually a resistent barrier to intra-thecal spread of the infection. Chronic epidural granuloma resultant from staphylococcal infection may give rise to delayed cord compression effects (Keith). Findlay and Kemp have noted the oc-

casional occurrence of vertebral osteomyelitis following lumbar puncture, presumably from needle trauma to the vertebral tissue. In such a case disintegration of one or more vertebral bodies may result. Radiographic evidence is absent in acute osteomyelitis until the periosteum has been denuded and sequestra have formed.

Complications.—Staphylococcal septicæmia is not unusual and is obviously a dangerous condition. It may be suspected by severe constitutional symptoms somewhat out of proportion to the local disease. Also acute anæmia, high swinging temperature, intestinal distension, a rising pulse rate, and persistent positive blood culture are in evidence. Secondary or further local acute disease may be set up so that multifocal osteomyelitis develops. Fulminating forms are so violent that death may occur in a few days. Damage to the hepatic renal and myocardial tissues should be kept in mind. Arthritis may be a benign passive effusion into the nearby joint and is usually of no great importance. Later pyæmic suppuration may occur in any joint. Pyæmic abscesses in the lung, with possibly pleural reaction and purulent effusion, are grave developments. Pericarditis may occur early; local pain may be absent but pericardial friction or even considerable effusion will be recognized. Pericarditis, with a moderate layer of purulent exudate, may be suspected from physical signs and ultimately a constricted pericardium may result. Ulcerative endocarditis with possibly coronary embolism, may occur. Residual effects may include an increased density of the shaft of the bone and a definite shortening of a limb.

Treatment.—The object of surgery in the acute phase is to drain the metaphysis without infringing upon the epiphysis or the medullary cavity. A small incision over the point of maximum tenderness down to and through the periosteum and the cutting of a narrow canal into the thin compact bone of the metaphysis allows the underlying cancellous bone to be drained and tension relieved. This treatment applied early may cause rapid lowering of toxæmia, and necrosis and subsequent sequestration minimized. Even in the absence of visible pus local bone fluid gives a culture of the staphylococcus. Surgery is often avoided entirely after early antibiotic treatment. Any subsequent surgery will of course depend upon the extent of bone necrosis and radiological evidence. At present chemotherapy should be considered as a valuable aid in the treatment of osteomyelitis when employed before extensive destruction of bone occurs; it doubtless will prove of great value in preventing some of the disastrous results observed in the past. In osteomyelitis with staphylococcæmia, combined treatment with sulphathiazole and penicillin may be more favourable. There is no doubt about the value of chemotherapy in this disease, but such does not entirely replace proper surgical and other measures such as fresh blood transfusions, diet, and general supportive therapy. The value of penicillin is now undoubted against most strains of staphylococci and some other micro-organism (Fleming *et al.*). Septicæmia osteomyelitis in specially dangerous sites, *e.g.* cranial bones, has been cured with penicillin (Williams and Nichols). Robertson records very encouraging results in acute

hæmatogenous osteomyelitis by the use of penicillin. Highly successful cases are reported in detail by Beales *et al.* Compere believes that penicillin should be given, 20,000 units three-hourly, day and night, and that the dose be reduced to 10,000 units three-hourly after the temperature has subsided. Robertson notes, however, that local application of penicillin in chronic bone sepsis has proved disappointing, probably due to difficulty in continuous application, possible inaccessibility of the bone infection and the presence of dead bone. In the presence of sequestra, penicillin treatment unaided by surgery has been unsuccessful; whilst sulphathiazole or penicillin may abort the acute infection a series of X-ray pictures taken some weeks later may show osteoperiosteal changes rather similar to that in sarcoma, hence the importance of correlating closely the radiology with the clinical history. As Hudson points out the radiographic changes in the "lag period" in the penicillin treated acute case, portrays the past events and must be considered in close relation to the present condition of the patient. Trueta considers that early cases can be treated by penicillin alone and might leave hospital perfectly normal after three weeks; for later cases surgery is still important and should include bone drilling and primary suture after evacuation of as much pus as possible, and immobilization of the affected part. Butler considers that penicillin therapy has reduced the mortality of acute osteomyelitis from 25 to 4 per cent.

Chronic osteomyelitis.—Low virulence of the infection and the absence of acute symptoms may lead to low fever and gradual thickening of the bone with possible sinus formation. The condition may be simulated by tuberculous infection or even chronic bone disease following typhoid fever.

Chronic bone abscess.—As in Brodie's original description, localized pain and tenderness, which may be supposed to depend on extreme tension, the pain being aggravated at intervals and having no relief from ordinary remedies, will make one reasonably suspect an abscess in the centre of the bone. It occurs most frequently in the metaphysis of a long bone. The clinical history will approximate to the age of the lesion. By X-ray examination the abscess may appear quite small or may be spatulate in form; the boundaries are not sharply defined, but demarcation with dense adjacent bone reveals its position. A small sequestrum may be observed in the abscess cavity. Such lesions as tuberculous abscess, simple bone cyst, sarcoma or endothelioma may have to be considered in some doubtful cases. Treatment of the chronic abscess is a simple surgical procedure.

Chronic subperiosteal abscess.—Brailsford (1942) finds a well-defined group in which the outstanding clinical features are bouts of pain in the affected extremity, in some little more than discomfort, in others sufficient to cause the patient to clench his teeth. A slight jarring may initiate a bout of pain. There may be no signs of inflammation or pyrexia and local swelling may only be present where the affected area of bone is relatively superficial. The symptoms develop insidiously and may persist for several years before a radiographic examination is made. The film shows a dense spindle-shaped expansion merging into the normal shaft above and below. This periosteal reaction may extend

all round a slender bone, *e.g.* ulna, or remain on one part of the circumference, *e.g.* the femur ; within this is seen the translucent abscess focus.

Osteomyelitis in infancy. It has been observed that the local disease is relatively benign in infants under two years of age. Simple incision down to an abscess may lead to quick and complete recovery. The rapid healing of the bone and the absence of sequestra is attributed to the thinness of the cortex and the loose attachment of the periosteum, pus thereby obtaining easy exit from the medulla to the soft tissues. By giving the infant fluids and immobilizing the affected limb until the general condition was satisfactory and then making a local incision down to the pus without disturbing the bone, Green treated thirty consecutive cases with only two deaths. Cass supports this view and indicates that in uncomplicated staphylococcal osteomyelitis in the newly born there is practically no systemic disturbance. In these cases the mother sought advice because of the swellings and not because the baby seemed ill. The pyrexia was slight, mild gastro-enteritis may occur and moderate anæmia develops. When the epiphyseal line is intracapsular there is a marked tendency to early joint infection because of the rapid escape of pus through the cortex, but surprisingly little deformity or disability usually follows. Considerable local destruction may result, however. Cases of osteomyelitis involving the hip-joint may be undiagnosed and be recognized later when pathological dislocation is discovered. Where the lower end of the femur or upper end of the tibia is affected, growth may be so affected to result in genu valgum or genu varus.

In *treatment* repeated aspiration of purulent material is more desirable than open incision and treatment with antibiotics is urgently required.

X-ray examination at a later stage may show subperiosteal osseous erosion resembling somewhat the appearances seen in congenital syphilis ; and irregular calcific foci may appear immediately beneath the separated periosteum.

Osteomyelitis of the maxilla is seen in infants, usually under twelve weeks, and may have progressed for several days before recognition. A prominence of the affected side with swelling and induration of the cheek, some fullness of the eyelids, a unilateral nasal discharge, and swollen and inflamed alveolus with narrowed bucco-gingival space indicate the process. The mandible may be involved and produce swelling mainly in the submental region. Remarkable and rapid resolution usually occurs by systemic penicillin (Jacoby observed complete cure in twelve days). Local surgical attention should be minimal and confined only to obvious collections of pus, and care taken to avoid damage to tooth buds.

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THE OSSEOUS SYSTEM AND LIPOIDOSIS

Osseous changes, especially cranial, are present in Schüller-Christian cholesterosis ; and lipoid infiltration may be significant in the earlier or later phases of Gaucher's disease. The association of visceral disorder and bone abnormality is now recognized in gargoylism.

Schüller-Christian disease.—In the Schüller-Christian syndrome, although the blood cholesterol is usually normal there is an osseous xanthomatosis in the membrane bones of the skull, and occasionally similar areas of intra-cellular deposition in other sites, *e.g.* ilia and ribs, spinal dura and skin. Pin-head xanthomas may be present in other tissues where reticulo-endothelial cells are normally present. Lung involvement may be considerable. Lymphadenopathy may be a prominent feature and typical lipoid granuloma is detectable in the enlarged lymph glands. Bouts of fever and arrested general growth may occur. The changes in the skull are characteristic, both clinically and radiologically. In an observed case aged eighteen months considerable areas of palpable bone defect were present in the parietal and frontal areas. There was no pain, but the eyes became variably prominent and severe thirst and polyuria developed. The cranial vault was rather large, suggestive of hydrocephalus. Radiographic examination in this disease may show the lipoid granulomatous process in any bone, but the calvarium is the special site of areas of almost complete decalcification, usually circular in shape or irregular and map-like in appearance. Bone regeneration may occur after radiographic treatment of the affected areas (fig. 526 and 527).

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Gaucher's disease.—The cerebroside kerasin accumulates in the reticulo-endothelial cells of the bone marrow and so causes destructive infiltration in the skeletal and hæmopoietic tissues. Involvement of the

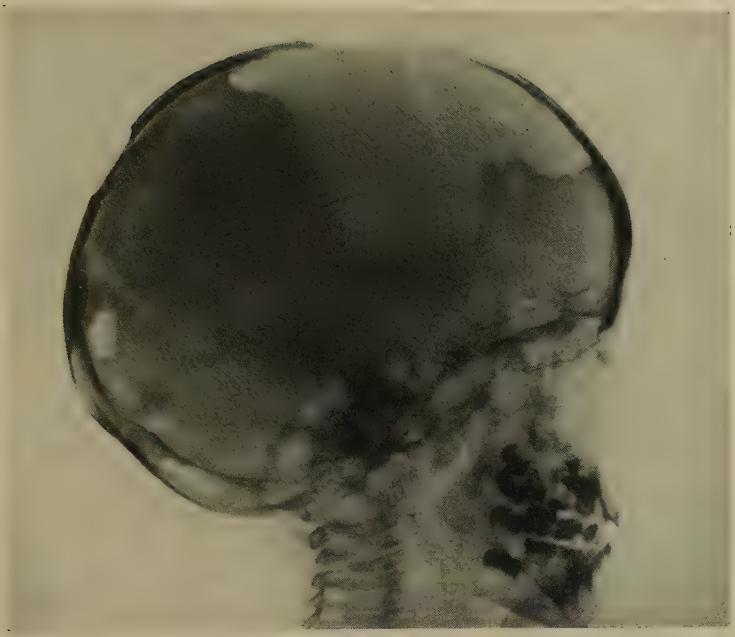

Fig. 526.—Hand-Schüller-Christian Disease.
Child aged three years. (Sir Leonard Parsons' case.)

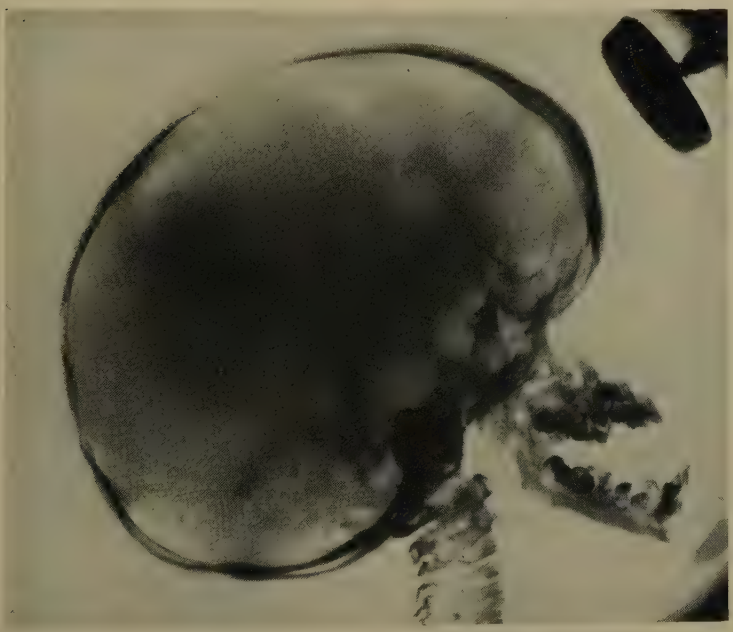

Fig. 527.—Same Case, aged Seven Years. After X-ray Treatment.

osseous system is as constant as the involvement of the spleen, and is one of the main features of the disease. The bone marrow contains white and yellow masses which may even simulate the appearance of pus. The osseous substance is rarefied and decalcified by the Gaucher cells. One characteristic feature is osteoporotic bulging of the distal third of the femur giving a radiographic picture like an Erlenmeyer flask. Similar changes may occur in other long bones. Destruction and collapse of one or more vertebræ may occur. Spontaneous fractures of bones occur in severe cases. Rarely the mandible or maxilla is involved. No changes are recorded of the skull. Some indication of the severe degree of bone marrow involvement in some cases is revealed by the occurrence of leuco-erythroblastic anæmia. The periosteum is usually spared and in fact may occasionally react by osteoblastic changes. Secondary arthritic involvement in early childhood may be wrongly interpreted as rheumatic disease and spinal deformity may present a picture similar to caries. Bone ache, pain and tenderness may simulate subacute osteomyelitis. Sternal marrow puncture is sometimes a useful diagnostic measure; Gaucher cells may be demonstrable in the aspirated material. Radiographic changes in the bones are indicated by decalcification, bone sclerosis, bone absorption and destruction, and deformities in the outlines of bones, especially the femur and the vertebræ. Pseudo-cystic areas may be seen. Osteosclerotic appearances may be found in the radius or ulna. The most impressive bone destruction occurs in the vertebral column where demolition of several vertebræ may occur. No case of Gaucher's disease has been described where the osseous system is involved exclusively.

FIG. 528.—OSSEOUS XANTHOMA.
Girl aged eight years, showing osseous xanthoma in the humerus. There were similar but smaller foci in the right fibula and in one vertebra. Serum cholesterol 280 mgm. per cent.

Osseous xanthoma.—A few rare cases have been described in which the skull, pelvis, scapula and long bones are the only location of xanthoma—limping and retardation of growth may be the only symptoms. Radiographic examination of the skeleton reveals smooth definitely circumscribed areas of bone rarefaction with almost no reparative signs. Biopsy may be necessary to confirm the diagnosis by demonstration of xanthomatous cells. In one case the child, aged eight years, had a spontaneous fracture of the upper third of the left humerus. X-ray showed a typical circum-

scribed cyst-like zone with thinning of the cortex. The serum, cholesterol, lipoids, calcium phosphorus, and phosphatase, are usually normal, but in this case the serum cholesterol was 280 mgm. per cent.

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GARGOYLISM

This is a relatively recent name which epitomizes a remarkable syndrome probably first recognized by J. Thomson of Edinburgh. Gargoylism is the term introduced by Ellis, Sheldon and Capon (1936) and is eminently descriptive of a variety of chondro-dysplasia exhibited by the "large head, grotesque inhuman facies, and deformed limbs rendering the patients closely similar and the condition easily recognizable." The same writers were the first to suggest that the disease might prove to be a disorder of lipoid metabolism. This form of osseous deformity is associated with clouding of the cornea, enlargement of the liver and spleen, mental deficiency, and dwarfism. The condition affects both sexes, although males predominate, and there is evidence of recessive inheritance. The disease has been observed in three members of a family on four occasions and it is apparent that there is a high familial incidence. "The most constant pathological changes are found in the osseous and nervous systems. In the brain there are widespread degenerative changes in the nerve cells with intra- and extra-cellular lipoid deposits. Lipoid deposit may occur in the cornea, liver, spleen and other tissues. The disease should be grouped with the congenital disorders of lipoid metabolism." The extra-cerebral lipoid deposit varies considerably in different cases. Recent work suggests that the abnormal material may be a glycoprotein. When the bone changes are generalized there is some resemblance to the Brailsford-Morquio type of osseous dystrophy. However, in the latter disease only skeletal changes occur, the head is normal, the trunk and limb deformities are much more extreme than in gargoylism and there is no mental defect.

Symptoms and signs.—Whereas the head in the Brailsford-Morquio dystrophy is little affected, in gargoylism the cranium is characteristic and nearly always enlarged, and hydrocephalus is frequent. Scaphocephaly or brachocephaly and less often oxycephaly and acrocephaly are noted. Unduly prominent supra-orbital ridges may occur and the eyes are prominent and widely separated. Closure of the anterior fontanelle is greatly delayed. Ross has pointed out the prominence of the skull above and posterior to the ears, which on X-ray examination reveals thinning of the parietal and temporal bones in that area. The grotesque face is one of the most constant features and an abnormally massive and prominent mandible may add to this. Dentition may be delayed and the teeth spacing will be wide apart and irregular. Coarse and bushy eyebrows

and some degree of hypertrichosis may be seen, but the hair is usually fine, dry and silky. The nasal bridge is flat and wide and the nostrils often turned forwards, and a purulent nasal discharge may be present. The ears are set low, and occasionally enlarged. The cheeks are full and may be ruddy. The lips are usually thick and the tongue may lie well forward and appear to be large and fissured. Considerable infantilism is evident. The neck is usually short and the chest seldom well formed, a minor degree of pigeon breast being frequent. The anterior ends of the ribs are expanded and the lower ribs are flared in association with the abdominal distension. Kyphosis in the lumbar or dorsi-lumbar region, usually with scoliosis, is detectable. Umbilical hernia and inguinal hernia are common. Some limitation of movement in the limbs is seen especially of extension at the shoulders, elbows and fingers. The fourth and fifth fingers may be incurved and the hands may be clawed. The relatively short arms and slight

FIG. 529.

FIG. 530.

GARGOYLISM.

Two sisters aged three and a half years and four and a half years.

(By courtesy of Drs. Ross, Hawke and Alan Brown ; and the *Arch. Dis. Childh.*)

permanent semiflexion suggests a crouching attitude and this is accentuated by the short neck and abnormally high scapulæ. The lower limbs may show limitation of extension at the knees, with some genu valgum or varum and coxa valga. The swelling round the joints described in the Brailsford-Morquio disease is not seen in gargoylism. Musculature is poorly developed, the abdominal muscles are weak, and the gait stiff and clumsy. Smooth and painless enlargement of the liver or spleen or both is present in most cases. The corneal clouding gives a ground glass appearance chiefly due to multiple opacities in the deeper layers. Both visceral and ocular abnormality may be absent. Mental deficiency is a characteristic feature and is usually obvious by two years of age, but may not be evident until a later stage. Deafness may contribute to the mental difficulties, and optic atrophy has been recorded in two cases.

X-ray examination of the skull often shows hydrocephalus and scaphocephaly. The sella turcica may be elongated, suggesting sphenoid

malformation. The vertebral bodies are irregular, flattened, wedge-shaped or somewhat ovoid, and appear small especially in the lower dorsal and upper lumbar region. The kyphosis is often related to one small vertebra, and usually the first lumbar, being squeezed back out of line of the others. In these various respects there is similarity with the Brailsford-Morquio disease but, however, there is not the same irregularity of the joint spaces and articulating surfaces in the other joints. The glenoid fossæ and acetabula are poorly formed and unduly shallow, and the humeral and femoral heads flattened or somewhat irregular; the metacarpals and the phalanges are shorter and broader than normal and may be very irregular and carpal ossification is retarded. Osteosclerotic and rarefied areas in the epiphyses are evidence of irregular epiphyseal ossification.

Diagnosis.—The mental impairment and the facies should clearly differentiate the condition from the Brailsford-Morquio disease despite possible similarity in osseous appearances. Gargoylism has been mistaken for cretinism. Thyroid deficiency might be suggested by the general picture, but thyroid medication has been of no real value.

Prognosis.—In common with other lipoidoses of childhood the outlook is poor. Survival beyond ten years is unusual. Several patients have lived longer and a few survived for more than twenty years.

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CHAPTER XXXI

ORTHOPÆDIC SURGERY

ERIC I. LLOYD

Introduction.—Orthopædic surgery plays an important part in the treatment of children. Considerable advances have been made and further important developments are likely in the near future. The treatment of poliomyelitis, congenital dislocation of the hip and spastic paralysis have all undergone alteration during the past generation and there are indications that limb-equalization operations are emerging from the experimental stage. A consideration of such problems or indeed any comprehensive survey of orthopædic surgery cannot find a place in this book, but there must be many occasions when the children's physician looks for help in dealing with the orthopædic conditions which he occasionally meets.

An approach to the subject is best made from the clinical rather than the pathological or anatomical direction. In the development of the child it is the act of walking that marks an orthopædic epoch. At this period the mammal becomes man, or at least anthropoid, and certain well-defined conditions make their appearance or for the first time become conspicuous.

We shall therefore consider the child under three age-periods ; at birth we find examples of transmitted characteristics and such states as result from the mighty hazard of reaching the world alive. At the onset of walking, there are defects that depend mainly on statics ; and in the last and longest age-period from four to twelve years we shall be confronted with the later effects of heredity, birth-injury and weight-bearing and, in addition, the results of accident and disease. We shall be guided by the period of life at which the condition is generally first noticed even though, as in congenital dislocation of the hip, it may have long existed unsuspected. Our present classification is simply a matter of convenience.

1. *CONDITIONS PRESENT AT BIRTH* [1]

Congenital deformities of almost every imaginable kind are occasionally met. A whole limb or a bone may be missing ; contractures of skin, muscles and even nerve, failure of normal fusion in the face, spinal cord or abdomen ; webbed fingers, extra fingers and toes, all these and many others occur. Splints can be used at an early age for some of these conditions and the surgeon is often content to defer operation until growth has widened the scope of plastic surgery and the function of the defective part can be better assessed.

Talipes or club-foot (fig. 531) is obvious at birth and that is the time to start treatment of the intractable equino-varus variety. Suitable manipulations and splints during infancy will often avoid operation in

[1] See also p. 260.

later years, and a painstaking parent or nurse can occasionally work marvels. Over-correction and not merely correction of the deformities must be the aim, and treatment even in successful examples should continue for years if relapses are to be avoided. Denis Browne's work has given mechanical means of treatment which are much more efficient than repeated manipulation and plaster of Paris. He has described three splints, *viz.* hobble splints, night boots, and, more recently, the calcaneus apparatus, which is probably the best of the three. These splints are excellent for maintaining correction, but manipulation morning and evening by the parent or nurse remains an essential part of the treatment and one which must be continued for many months. The neglected feet of older children must be corrected by tenotomy, tendon-transplantation or arthrodesis, but the performance of such operations is often a condemnation of the child's management in earlier years. None the less, almost any foot can ultimately be made serviceable at some sacrifice of mobility, appearance, time and trouble.

Talipes calcaneo-valgus is more tractable and can usually be success-

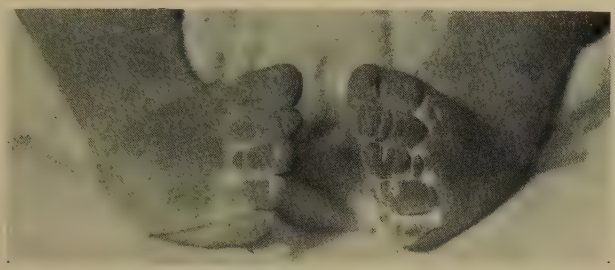

FIG. 531.—TALIPES EQUINO-VARUS, UNTREATED.

fully treated by manipulation into the opposite position of equino-varus followed by a straight malleable splint along the antero-lateral aspects of the leg and foot or a flattened-out hobble splint along their inner surfaces or by Browne's valgus " bootie."

SPASTIC " PARALYSIS " (" cerebral palsy ") forms a large and difficult group of orthopædic problems. The cause used to be thought to be intracranial hæmorrhage in most cases, but it is now believed that such disasters are usually fatal within a few days and that the probable causes are cerebral asphyxia or mal-development which may be often associated with prematurity, and perhaps sometimes with minor hæmorrhages. The exact part played by the Rh factor (p. 1253) in causing such paralysis is still unsettled.

The " paralysis " may be monoplegic, hemiplegic, paraplegic or diplegic, depending on the exact situation of the lesion and it has been seen (p. 215) how these conditions may be suspected from the asphyxia, lethargy or convulsions of the infant during the first few hours of life and before the onset of the characteristic spasticity. Such children may suffer from fits, athetosis or a mental defect which makes operation inadvisable, but it is often possible in the milder examples to do something to make them less

FIG. 532. — TALIPES EQUINO-VARUS, SHOWING FULL CORRECTION.

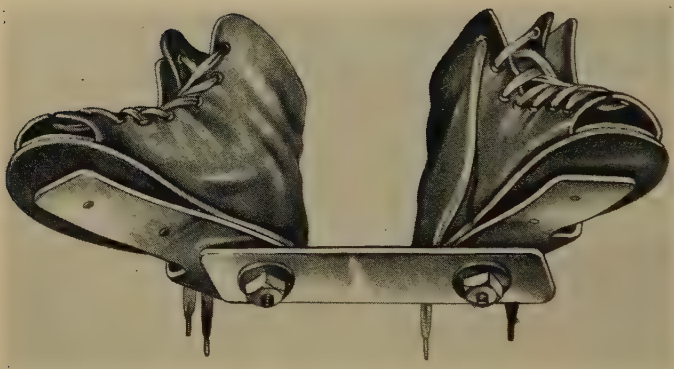

FIG. 533.—DENIS BROWNE'S NIGHT BOOTS FOR TALIPES EQUINO-VARUS.

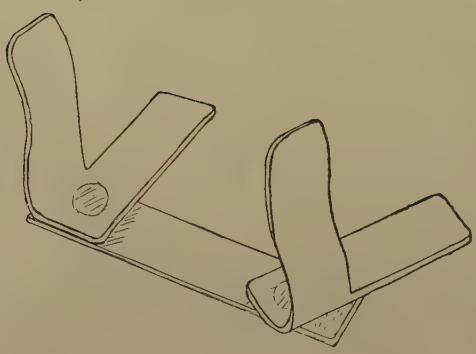

FIG. 534.—DENIS BROWNE'S HOBBLE SPLINT.

(Fig. 532-4 from *Royal Northern Operative Surgery*, H. K. Lewis and Co.)

dependent on others. In particular, when a child has learnt to sit but cannot walk, the time comes when neurectomy (Stöffel's), tendon lengthening or tenotomy will aid the all-important educational exercises. The obturator nerve may be excised, the tendo Achillis lengthened, the hamstrings divided and the superior gluteal nerve cut with benefit to suitable patients. Re-educational exercises, however, remain the foundation of treatment and neither splint nor operation can supplant them. Massage and electricity must be avoided and progress, even at the best, is slow. A routine Wassermann test is the rule, but antisyphilitic treatment seems to do little for such children, even on the rare occasions when the test is positive. In the mild examples of spastic paraplegia which obviously do not call for surgical treatment, a long rectangular night-shoe or Browne's calcaneus apparatus is essential if there is the slightest tendency to equinus of the foot, and a moulded leather splint to the wrist will do something to prevent the disabling contracture so commonly seen in the adult hemiplegic. Winthrop Phelps, Earl Carlson and other American workers have drawn attention to the great importance of training and education in these cases and some serious attempts are now being made to grapple with the problem in this country. Phelps maintains that athetosis is by no means always unfavourable and distinguishes between "tension and non-tension athetosis." Evans at Carshalton found that over 90 per cent. of the patients with athetosis are educable and it is quite apparent that we are not sufficiently alive to the importance of accurate diagnosis in these cases.

OBSTETRICAL PARALYSIS affects the upper limb and follows a tension strain on the brachial plexus during birth. The commonest form (Erb's palsy) produces a paralysis of the muscles supplied by the upper two trunks and the limb hangs internally rotated by the child's side. The whole arm type (Klumpke) is less common and the damage to the nerves more widespread. Fortunately, complete nerve division is rare and a large amount of recovery follows the application of suitable splints which should be applied early and worn day and night. The treatment of these patients is prolonged and in spite of every care there may be a residual deficiency of external rotation of the shoulder, extension of the elbow and supination of the forearm. In the later or badly treated examples there is hope of improvement from operation, but an early diagnosis goes far towards a good result. Subluxation of the shoulder or of the head of the radius is liable to follow contracture of unopposed groups of muscles.

Another accident of birth is the so-called STERNO-MASTOID "TUMOUR" which can be felt as a hard swelling in the lower third of the sterno-mastoid muscle of one side. The birth has often been abnormal and a breech presentation is so common that interference with the vascular supply of the muscle may well have occurred. Probably the condition is often overlooked, as it generally produces no symptoms at the time. The localized swelling usually disappears within a few weeks of birth and no treatment is necessary, though the possibility of subsequent torticollis must be remembered (p. 1524).

Cephalhæmatoma is another birth injury which recovers without treatment, but careful examination is always necessary to exclude a depressed fracture of the parietal bone.

Birth fractures will be noticed in a later section (p. 1521).

2. *CONDITIONS APPEARING WITH THE ONSET OF WALKING*

Rickets has been considered elsewhere (p. 277) and it need only be mentioned here as an important cause of certain well-known deformities. Rickety bow-legs and spinal curvature are examples and it is obvious that the general treatment of the condition is quite as important as that of the local abnormality.

Flat foot scarcely exists in childhood, but the common painless condition of everted feet (valgus ankles) often wrongly goes by that name. Here, the erect attitude finds the inverting muscles of the foot (tibialis anticus and posticus) at first unprepared for the strain of weight-bearing, but a wedge of $\frac{1}{6}$ inch to $\frac{1}{4}$ inch on the inner side of the shoe and a short course of exercises will soon establish equilibrium in the foot. A true flat foot does occasionally occur even in children, and is then due to some congenital abnormality of the bones (such as a vertical astragalus), muscles or ligaments. Exercises should be prescribed and may have to be supplemented by some form of arch support and occasionally even by operation in older children.

Knock-knee (genu valgum) is common and is usually wrongly attributed to rickets. The condition is a purely mechanical consequence of the valgus ankles which are associated with the beginning of walking. Knock-knee and valgus ankles almost always co-exist and are cured in their milder degrees by the simple mechanical device of moving inwards the line of weight transmission by an inside lift or wedge to the shoe. Severer grades of knock-knee call for a night splint or metal brace which must be worn by night as well as by day. Supracondylar osteotomy (Macewen) followed by plaster of Paris for six weeks was for long the correct treatment when these methods had failed, but epiphyseal stapling may take its place before long in older children. Albuminuria in a child with knock-knees indicates renal inadequacy and operation is then dangerous, because uræmia may follow anæsthesia and there is only a remote chance of the child growing up.

Bow-leg (genu varum) occurs less frequently than knock-knee. It is common in the form of the curved tibiæ of infants but only occasionally results from deformity of the femur. Both forms of bow-leg are sometimes rickety and are curable by splints or operation.

Congenital dislocation of the hip exists from before birth, but it usually escapes detection until the child begins to walk, when the unusual dip or waddle attracts attention. Asymmetry of the creases on the inner side of the thighs or shortening of one lower limb in a baby girl may hint the truth at a much earlier age. Suspicion once raised makes diagnosis easy and X-ray examination puts the matter beyond doubt. The results of treatment depend partly on the age at which it begins but arthrograms

FIG. 535.—VALGUS ANKLES WITH PATIENT SITTING.

FIG. 536.—VALGUS ANKLES AND KNOCK-KNEE WITH PATIENT STANDING.

(Fig. 535 and 536 reproduced by kind permission of *The Practitioner*.)

may help to distinguish dislocations from subluxations and clarify the indications for open reduction. The dislocation is reduced by traction or manipulation and treatment in plaster of Paris continues for about twelve months. Open operation is reserved in this country for those occasions when other methods have failed, but the older children whose dislocation has recurred or been overlooked present a difficult problem to the orthopædic surgeon. There are occasions when a bone graft or osteotomy is indicated, but there are others when the child is best left alone.

3. *CONDITIONS APPEARING IN LATER CHILDHOOD*

Poliomyelitis may occur at any age, but is best considered here. Although certain aspects of the disease have been discussed elsewhere (p. 1299) it is important to realize that orthopædic treatment begins with the onset of paralysis. The surgeon can prevent certain deformities much more easily than he can cure them, and plaster of Paris for six weeks may forestall a multiplicity of operations. We must first decide what muscles or groups of muscles are affected and then plan how to put them at rest. This is done by splint or plaster specially adapted to the needs of each patient, with special reference to the prevention of deformities which gravity, posture and the action of unopposed healthy muscles so rapidly produce. Deformities which are common in badly treated poliomyelitis are almost always the result of the preventible contractures (*i.e.* shortening) of healthy muscles and it is deplorable to allow a child to develop them. No one can be blamed for a flail foot which is at right angles to the leg and midway between varus and valgus, but if the same foot has been pushed by bedclothes and pulled by unopposed calf muscles into a position of fixed equino-varus it is because somebody has allowed it to happen. Similar arguments apply with equal force to every joint in the body.

Prevention of deformity is therefore the great guiding principle in the early paralytic stage of poliomyelitis, but before we can make our plans to help the muscles we must first know which are paralysed. This entails a careful examination of the individual patient, not forgetting the back and abdominal musculature. Having decided which muscles are paralysed we proceed to apply the second principle that *physiological rest in a muscle is secured by anatomical approximation of its two ends.* This dictates the position which our splint or plaster must maintain and we shall be safe in leaving the patient in this position and at rest in bed for a period of six weeks. At the end of that time pain and tenderness will have disappeared and the third principle now becomes important ; *an affected muscle benefits from work which stops short of overtiring it.* Herein lies the reason for graduated exercises, swimming baths, walking apparatus and night splints for the patient ; and for his doctor and masseuse a little mechanical, and a lot of common, sense.

Treatment in this stage therefore means exercise but not over-exercise and it should continue for two years, or longer if natural recovery is still

proceeding. Two years is an arbitrary period and operations are rarely advisable until that time has elapsed. When all natural recovery has ceased, it is time for the surgeon to count the patient's assets and decide how they can be most profitably distributed. It is true that earlier operation may be occasionally justified, but this is usually in the untreated or ill-treated example where gross contractural deformities must be corrected before the paralysed muscles have even a chance to show what they can do. We must decide not only how much is left but also how it can best be used. A tendon transplantation may restore balance, tenotomy liquefy frozen assets and arthrodesis stabilize a currency.

Fractures.—The diagnosis and treatment of children's fractures differ slightly from those of adults. Their special features are the presence of un-united epiphyses, which may become displaced when an adult bone would fracture, the occurrence of bending rather than breaking in a young and incompletely calcified bone (greenstick fractures), the remarkable powers of adaptability and the tendency of growing bone to unite rapidly. Apart from epiphyseal injuries, the only fractures peculiar to children are obstetric and " congenital pseudarthrosis." The former are commonest in the femur, clavicle and humerus and present no special difficulties as they unite quickly and certainly. The latter occur almost always in the tibia and their extreme reluctance to unite is notorious : a by-pass bone graft (McFarland) may avoid amputation. Exact diagnosis of all fractures depends on X-ray examination which does not, however, show cartilage, so that it is necessary to have some knowledge of the normal appearance of bones at different ages. Fractures of the lower end of the humerus are particularly important, and may lead to ischæmic contracture of muscle (Volkmann). This noteworthy condition is now known to be due to segmental spasm of the main artery to a limb accompanied by reflex spasm of the collateral circulation. The best safeguard is immediate reduction of the fracture with avoidance of acute flexion and of any constriction in front of the elbow-joint. Signs of impending ischæmic contracture are increasing pain and swelling in the hand, absence or diminution of the radial pulse, with increasing flexion of the fingers and diminishing power of extension. An attempt to relieve the spasm of the collateral circulation should be first made by putting the child in a warm bath with the injured limbs uspended above it. If this is unsuccessful it is probably best to excise the part of the brachial artery which is in spasm, but the operation must not be too long delayed as irreparable damage may be caused in a few hours. Volkmann's contracture treated by gradual correction with splints or by operation always leaves some permanent disability, so that prevention when possible is a most urgent matter.

Scoliosis.—Alterations in the normal line of the spine are common in children. Lateral deviations (spinal curvature or scoliosis) are produced in many ways and the spinal condition is in nearly all of them secondary to some other abnormality although " congenital " scoliosis is due to some bone abnormality, most often a wedge-shaped vertebra. Examples of secondary scoliosis are provided by poliomyelitis, torticollis, empyema

and the common congenital shortness of one leg. There remains a large group in which no cause can be demonstrated and we are forced to assume faulty posture, rickets or undetected poliomyelitis. The outlook depends largely on whether the curvature is postural (*i.e.* corrects itself on suspension or trunk-bending), or structural (*i.e.* incorrectible by the above). Remedial exercises, particularly Klapp's crawling exercise, are indicated in both groups, but plaster beds, spinal supports and perhaps fusion operations find a place in the severer grades of the second group.

Kyphosis and lordosis.—Antero-posterior abnormalities of the spine

Fig. 537.—Adolescent Kyphosis with Tight Hamstrings.

are less common than lateral deviations and are not infrequently due to vertebral tuberculosis (Pott's disease).

The less acute forms are the " round shoulders " of childhood, which may progress to an actual kyphosis ; and the lumbar lordosis, which is often secondary to abnormalities of the hips, paresis of the gluteal muscles or to a lax abdominal musculature.

Abnormal inter-vertebral discs are now thought to be an important cause of kyphosis and especially of that form known as adolescent kyphosis, which begins in late childhood but whose effects continue throughout life. It is believed that either these discs or the epiphyseal plaques of the vertebræ themselves are the structures from which the process arises and that probably those children who have tight (*i.e.* short) hamstrings are

particularly prone to kyphosis. It thus becomes important to see that such patients are not subjected to the strain of toe-touching exercises which in them increase the dorsal kyphos instead of flexing the pelvis on the thighs (fig. 537). Treatment, apart from prophylaxis, aims first at mobilizing the dorsal spine and later at strengthening the muscles which maintain full extension. A plaster bed at night and a spinal brace by day are sometimes necessary in severe examples.

Perthe's disease (pseudocoxalgia).—This condition is most commonly noticed in children during the second five years of life when it may be mistaken for tuberculosis of the hip. It is important to distinguish between the two and the following table shows some of the chief points :

	Pseudocoxalgia	Tuberculosis of hip
Age of onset . .	5–10 years	1–5 years most commonly
Chief symptoms . .	Limp and pain	Pain and limp
Movements of joint limited	Abduction and rotations	All directions
Mantoux test . . .	Negative	Positive
Sedimentation rate . .	Normal	Raised
X-ray examination . .	Characteristic changes (see below)	Only general rarefaction in early cases

The earliest radiological change in Perthe's disease is a slight flattening of the outline of the upper epiphysis of the femur. The later changes include widening and fragmentation of the epiphysis ; widening and cavitation of the neck of the femur and an apparent increase in the joint space of the hip.

Treatment ideally consists in full relief from weight-bearing for as much as two or three years but some compromise on this may be often permitted. The condition may be followed by an early osteo-arthritis of the hip if a normal joint is not ultimately obtained but there is no risk to life.

Coxa valga and coxa vara.—Coxa valga is present when the angle which the neck of the femur makes with the shaft exceeds 124° and coxa vara is the opposite deformity. The former is of little surgical importance and occurs principally in those children who have never walked. Coxa vara deserves further notice :

There are three principal forms :

(1) The rachitic, which occurs in young children who show other signs of rickets. There is a general softening of the bones, and weight-bearing leads to bending of the femur with diminution of the angle of the neck.

(2) Adolescent, in which the upper femoral epiphysis slips downwards on the adjacent neck. This occurs in two forms :

(*a*) A sudden slip following a single and moderately severe injury ;

(*b*) A gradual slip which may be bilateral and whose ætiology is unknown.

(3) Infantile or cervical, whose principal characteristic is in the X-ray film, which sometimes shows a triangular portion of bone in the lower part of the neck of the femur.

The diagnosis of coxa vara rests finally upon the X-ray appearances, but the clinical signs are a limp with little or no pain, elevation of the

great trochanter and limitation of abduction and internal rotation of the hip joint.

Treatment depends on the variety of coxa vara and is beyond the scope of the present survey.

Torticollis.—Torticollis or wry-neck has many local causes which may determine a more or less sudden onset: amongst these are cervical adenitis, mastoiditis and fibrositis. An X-ray examination may reveal tuberculosis of the cervical spine or congenital abnormalities of the bone. Ocular torticollis occurs rarely. In most of the children affected with torticollis the sterno-mastoid muscle on one side is obviously tight, giving the head a tilted and twisted appearance which sometimes co-exists with facial asymmetry. This is the so-called congenital torticollis, which is probably a late result of birth trauma and seems to be associated with the sterno-mastoid "tumour" previously mentioned. Tenotomy of the affected muscle is usually necessary, though it is best postponed until the child is aged three to five years. The structures divided at operation may have to include the carotid sheath and after-treatment by posture and exercises must be carefully given. The outlook is excellent in well-treated examples.

There is a second and less common form of congenital torticollis ("postural") which is present at birth and usually recovers without operation. It is probably the result of intra-uterine compression.

Fig. 538.—Congenital Sterno-mastoid Torticollis.

Slight facial asymmetry and tight left sterno-mastoid muscle.

Osteomyelitis.—Syphilis and tuberculosis have been considered elsewhere, but we must refer briefly to the pyogenic infections of bone. Inflammation of bone is almost always a blood-borne infection which may be staphylococcal from the skin, streptococcal from the tonsils, or pneumococcal from the lungs. The first named is the commonest and most lethal. Injury certainly plays a part and the long bones most exposed to injury are those most often affected by osteomyelitis.

The disease starts in the metaphysis, which is the most vascular part of the bone and which lies on the diaphyseal side of the epiphyseal cartilage. The inflammation remains pent up in this area for a time and osteomyelitis may be diagnosed with confidence if a toxic child is acutely tender to pressure over one of these areas.

It is important to distinguish the early stages of osteomyelitis from

acute rheumatism, and time is such an important factor that it must not be lost in awaiting the effect of salicylates.

Articular rheumatism is articular and osteomyelitis is not. Rheumatism runs from one joint to another while osteomyelitis is stationary. Rheumatism may kill in a month, but osteomyelitis in a few hours: therefore the diagnosis is important.

The discovery of penicillin and the sulphonamide drugs has revolutionized the treatment of osteomyelitis and reduced the mortality to about one-tenth of what it was previously. Penicillin is usually given systemically into the vastus externus or upper and outer quadrant of the buttock and eight doses of 50,000 units at three-hourly intervals should be given in every twenty-four hours for six or seven days. Infants should receive 2,000 units per lb. expected body-weight per twenty-four hours in six doses. No time should be lost in starting to treat a suspected case but a careful examination for abscesses must be made and repeated daily because the drug can only act via the blood stream. Any such abscesses should immediately be aspirated and the fluid sent to the pathologist for identification of the organism and an estimate of its penicillin-sensitivity.

Operation is rarely nowadays necessary in the acute cases, but this is not true of the chronic forms where the infection is usually isolated by thrombosis and is thus inaccessible to penicillin.

Fortunately, nearly all cases of acute osteomyelitis respond very well to penicillin therapy provided always that it is started early enough, given in adequate doses and continued for a sufficient time. The disease may still cause death from dangerous complications (such as endocarditis) if any of these requirements is not fulfilled.

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CHAPTER XXXII

MEDICAL DISEASES OF THE URINARY SYSTEM

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THE high incidence in childhood of disease of the genito-urinary organs, notably acute nephritis, pyelitis and disorders associated with congenital malformations, demands a renal and urinary investigation as a necessary part of the routine examination of a sick child. This examination is made doubly necessary in regard to prognosis and treatment by the alterations in kidney function which occur so commonly in diseases not primarily renal in origin. Thus, the renal damage which accompanies circulatory failure, as seen in shock and the dehydration following severe diarrhœa, affects both outlook and management. Similarly, in the correction of electrolyte imbalances, so often seen in disease in infancy, the part played by the kidneys must be given full consideration.

THE NORMAL KIDNEY

A proper understanding of kidney disease and its effects upon the body requires some knowledge of the intricate mechanisms of the kidney. Though these mechanisms are not fully elucidated, it is possible to give an account which, despite its imperfections, may serve as an introduction to the subject.

Each kidney consists of approximately 1,000,000 functional units or nephrons, with their blood supply and supporting tissue. Each nephron is formed of a tubule 4 to 5 cm. in length, whose upper, blind extremity is invaginated and distended by a tuft of capillaries, the glomerulus, to form a capsule, Bowman's capsule, lined by flattened epithelium and situated in the renal cortex. From the neck of this capsule the tubule, now lined by columnar cells, pursues a tortuous course in the renal cortex, forming the first or proximal convoluted tubule. It then forms a loop - Henle's loop—with relatively straight limbs descending into and returning from the medulla. The descending and ascending limbs of the loop are lined by columnar or cuboidal cells, while the intervening portion is narrowed and lined by flattened epithelium. At the upper end of the ascending limb the course of the tubule again becomes tortuous as, lined by columnar cells, it becomes the second or distal convoluted tubule, which ends close to the glomerulus from which it arose by opening into a collecting tubule. Collecting tubules from several nephrons fuse into larger tubules, and this process is repeated several times to form ultimately a small number of short, wide tubules—the ducts of Bellini—which open at the apices of the pyramids into the renal pelvis. Just before joining the collecting tubule, the distal tubule comes into close relationship with the afferent arteriole of the glomerulus, and at this point its wall

is thickened to form a "macula densa." The nephrons whose glomeruli are situated in the deep cortex—juxta-medullary—differ from the remainder in that the glomeruli are larger while the loops of Henle are much longer, extending deeply into the medulla and having much longer thin-walled segments.

In the fœtal kidney the cells lining Bowman's capsule are cuboidal, and the change to flattened cells occurs after birth. The lowered permeability of the cuboidal cells may be associated with the low filtration of the neonatal period.

Each nephron is supplied by an afferent glomerular arteriole arising directly from a relatively large branch of the renal artery, a fact of considerable importance as it results in the intra-arteriolar pressure being considerably higher than in arterioles elsewhere in the body. This afferent arteriole comes into close relationship with the macula densa of the distal convoluted tubule, and at the point of contact the wall of the arteriole is considerably modified. To the area of contact where the walls of arteriole and tubule are modified is applied the term "juxta-glomerular complex." The afferent arteriole enters the glomerulus and breaks up into a leash of capillary loops, each clothed with an extension of Bowman's capsule, and the distal ends of the loops unite to form the efferent glomerular arteriole, a vessel with a calibre of less than half that of the afferent vessel. The efferent vessel divides to form a second meshwork of capillaries which invests the tubule of the same nephron, and these capillaries unite to form veins which, after various further fusions, drain into the renal vein. In the juxta-medullary region, however, the vascular arrangements are different. The efferent arterioles from the glomeruli are vessels of larger calibre, and each divides quickly to form a leash of large vessels—the arteriæ rectæ—which pass vertically into the medulla and then loop back at different levels as the venæ rectæ which end in the juxta-medullary region by joining tributaries of the renal vein. These straight vessels lie in close relation to the loops of Henle. Thus, virtually the whole of the blood reaching the kidney passes through glomerular capillaries, and the majority then circulates through a further series of capillaries in relation to the convoluted tubules before reaching the renal vein. A smaller proportion, however, passing through the juxta-medullary glomeruli, travels thence to the renal vein more directly through wide calibre vessels. The possibility exists also of other more direct communications between the renal artery and vein.

Trueta and his colleagues have demonstrated that in animals suitable nervous stimulation causes great diminution of blood flow through the cortical glomeruli, while the circulation through the juxta-medullary glomeruli is increased. They believe that this shunt is an important feature in certain pathological conditions in man, as in traumatic shock and after rapid hæmorrhage.

In relation to its size the kidney receives a large volume of the circulating blood, approximately one quarter of the cardiac output being normally divided between the two kidneys. The control of the renal circulation is under the influence of both nervous and hormonal influences,

and it appears that differential constriction can occur in the main renal artery, its larger branches or the afferent or efferent glomerular arterioles. Other things being equal, the circulation of the kidney as a whole is increased by a rise in systemic blood pressure and vice versa. When, from nervous stimulation, there is a reduction in renal blood flow, it often happens that diminution of flow is seen first in the superficial cortical glomeruli. As the stimulation is increased the blood flow through the superficial glomeruli is further reduced, while progressive layers of cortical glomeruli become involved, and with intense stimulation there may be complete cessation of blood flow in large numbers of cortical glomeruli.

Formation of urine.—The initial process in the formation of urine is one of simple filtration from the glomerular capillaries into Bowman's capsule of a protein-free liquid, identical in other respects with plasma. The quantity filtered each twenty-four hours is very considerable, being 4 to 5 litres in a newborn 3·5 kgm. infant, and increasing with age until the adult figure of 180 litres is reached. During the passage of the filtrate down the tubule it is considerably modified and converted to urine, chiefly by a process of differential absorption. About 99 per cent. of the water is absorbed, rather more than half of this absorption occurring in the proximal tubule. The solutes may be divided into three groups as regards their absorption. In one group, containing glucose and certain ions, notably sodium, potassium, chloride and phosphate, active absorption occurs: thus normally the whole of the glucose and most of the sodium and chloride are absorbed, the absorption of the glucose and sodium occurring in the proximal tubule, and the chloride in both proximal and distal tubules. The second group is typified by urea, and in it absorption is by a process of simple diffusion. The third group is of substances, such as inulin, mostly foreign to the body, which are completely unabsorbed. Active tubular excretion normally plays little part in the formation of urine, but a few substances, notably diodrast, are eliminated largely in this way. While the composition of the fluid is altering during its passage down the tubule, so also is its reaction changing, the change being commonly from a *p*H of 7·4 to one of 6·0. With this change in reaction there occurs a change in the ratio of monobasic to dibasic phosphate ($H_2PO'_4$ to HPO''_4), and also of the ratio of bicarbonate to carbonic acid. One other important tubular mechanism is that of the formation of ammonia from amino acids; the ammonia formed "covers" acid radicles being excreted and enables the body to retain fixed base, especially sodium.

Control of urine formation.—Many factors influence the flow and composition of urine, and these can be divided into two groups, those affecting filtration and those affecting reabsorption.

(A) Factors affecting filtration

(1) *Systemic blood pressure.*—Other things being equal, a rise in systemic blood pressure will increase the filtration rate and vice versa.

(2) *Local circulation.*—A rise in pressure within the glomerular loops or an increased rate of blood flow through them, brought about by nervous or hormonal factors, will increase the filtration rate.

(3) *Plasma protein.*—A lowering of plasma osmotic pressure caused by a fall in plasma proteins will lead to a rise in filtration rate.

(4) *Tubular reabsorption.*—Fluid reabsorption in the tubules, by removing the fluid molecules adjacent to the walls, lowers the resistance to passage of fluid through the tubules and thereby the intracapsular pressure. Increased tubular reabsorption thus leads to increased glomerular filtration.

(B) Factors affecting tubular reabsorption

(1) *Changes in the chemical composition of the circulating blood.*—As the kidney is one of the essential organs for maintenance of the chemical stability of the body fluids, it is to be expected that changes in the composition of the blood will lead to urine changes, and this is accomplished chiefly by differential tubular reabsorption. Thus, a tendency to acidosis leads to increased retention of base by the kidney and the excretion of a more acid urine; in this process phosphate is excreted chiefly in its more acid (monobasic) form, bicarbonate is almost entirely absorbed, there is an increased excretion of organic acid, and there is a large increase in output of ammonia by the tubule cells, covering the acid radicles and allowing absorption of fixed base. On the contrary, metabolic alkalosis leads to diminished absorption of bicarbonate and of sodium ions, a change of phosphate to the dibasic form and a diminished ammonia production. A fall in the blood content of sodium or chloride, as may occur in severe gastro-intestinal disturbances, leads to increased tubular absorption of these ions, and a complete disappearance of chloride from the urine is one of the tokens of severe chloride loss, as may be seen in untreated congenital pyloric stenosis. In addition to defending the levels in the blood of individual ions the kidney attempts to maintain the normal osmotic pressure of the blood, and this mechanism takes precedence over that for defence of *p*H previously mentioned. Thus, in the alkalosis of severe vomiting the kidney may secrete an acid urine, owing to excessive reabsorption of base in an attempt to maintain osmotic pressure in the face of heavy losses of electrolytes in the vomitus.

(2) *Hormonal effects.*—The renal tubules are under continuous control by many hormones, one of the most important of which is the anti-diuretic hormone of the pituitary, which promotes tubular absorption of water. This normally maintains a most delicate balance, and a very slight dilution of the blood stimulates "osmoreceptors" situated in the vascular territory of the internal carotid artery; nervous impulses from these inhibit secretion of pituitary hormone, and there follows a diminution of absorption of water in the tubules so that diuresis results. The great diuresis which follows failure of formation of this hormone is seen in diabetes insipidus. Water absorption is controlled also to some degree by the hormones of the suprarenal cortex, and these hormones are of first importance in the control of sodium and potassium reabsorption; destruction of the suprarenal cortex leads to loss of sodium and retention of potassium by the kidney, while the reverse effect is seen in certain suprarenal tumours. Phosphate absorption is under the control of the

parathyroids, and the primary effect of excessive secretion of these glands is increased phosphate loss.

The kidney and arterial pressure.—Although the association of kidney disease with raised arterial tension was recognized by Bright, many generations passed before a reasoned explanation for this association could be given, and it is only recently that the kidney has been accepted as an organ concerned with physiological as against pathological changes in arterial tension. Goldblatt first showed that restriction of the blood flow to a kidney led to hypertension by chemical mediation, and it is now known that anoxic kidney tissue is the sole site of formation of two substances, V.E.M. (vaso-excitor material) and renin, concerned with arterial tension. V.E.M. is intimately concerned with peripheral circulation, and causes constriction of vessels peripheral to the arterioles. Renin combines with a plasma globulin, hypertensinogen, to form hypertensin, a substance responsible for arterial hypertension. Fully oxygenated kidney tissue produces enzymes which destroy both V.E.M. and hypertensin.

In passing, it may be noted that there are three different associations between arterial hypertension and renal disease ; in acute nephritis both the hypertension and the renal damage are the result of a common cause, in chronic nephritis and other kidney diseases in which portions of renal substance are partially deprived of blood supply hypertension is the direct result of renal damage ; while hypertension from other causes can result in kidney disease. When one is faced with the end results, clinical and pathological, of the interplay of these various mechanisms, attempts to reconstruct the sequence of events may be fraught with the greatest difficulty, and it is not surprising that understanding of the morbid processes of Bright's disease and hypertension has come but slowly.

Normal urine

The daily quantity of urine varies from child to child, and from day to day in any child ; it is affected by the fluid intake, the temperature and humidity of the environment, and by exercise ; any pathological loss of fluid by other routes, as in diarrhœa, will lower the urinary output. Under ordinary circumstances it amounts to about half the fluid intake and rises with age. Thomson has investigated the urine output in the neonate, and finds considerable variation, dependent partly on the weight of the infant and partly on the time of establishment of feeding. The average output rises from 20 c.cm. (range 0 to 68) on the first day to 147 c.cm. (range 40 to 302) on the seventh. Camerer estimates that the normal infant during the first year of life excretes about two thirds of its fluid intake by the kidney. In later childhood the following figures, taken from the combined results of various investigators, represent the average daily amount of urine in health : 15 ounces at two years ; 20 ounces at four years ; 30 ounces at seven years ; 40 ounces at twelve years.

Chemical composition.—Except in early infancy, the urine of the child is chemically similar to that of the adult, and reflects the various normal nutritional processes. The largest single normal constituent, and

that which normally has the greatest effect on the specific gravity, is urea, commonly present in from 1 to 2 per cent. Chloride ranks next, with a concentration, expressed as sodium chloride, fluctuating around 0·5 per cent. Other ions present in smaller but measurable quantities are those of sodium, potassium, magnesium, phosphate and sulphate. Ammonia is present in acid urine, and bicarbonate in alkaline urine, while free carbon dioxide is usually present in the same partial pressure as in the blood. Apart from urea, other organic constituents include uric acid, especially abundant in the neonatal period when "uric acid infarcts" may occur, small quantities of amino acids, creatinine and creatine, the last being absent from normal adult urine. Glucose is normally absent from the urine, but a transient and unimportant glycosuria may occasionally occur, as after Rammstedt's operation for pyloric stenosis.

Although the total solid content is normally lower in the child than the adult, the child's kidney, except in early infancy, has the same concentrating powers as that of the adult, and deprivation of fluid can readily lead to the secretion of urine with full adult figures. In the neonatal period, however, the tubular function is imperfect, and concentrating powers are lower. Thomson records an average chloride level of 0·25 per cent. (range 0·1 to 0·6 per cent.) on the first day, falling to 0·16 per cent. (range 0·05 to 0·4 per cent.) on the seventh; while urea fell from 0·7 per cent. (range 0·25 to 1·5 per cent.) on the first to 0·25 per cent. (range 0·1 to 0·5 per cent.) on the seventh. Tubular function improves rapidly during the first few months of life, and probably reaches adult values before the end of the second year.

Reaction.—Although the *p*H of the urine of a child may, as in an adult, vary in health between the wide limits of 4·8 and 8·0, it is seldom that these limits are approached, and in the normal child on an ordinary diet a *p*H of 6·0 is commonly recorded, the urine being just acid to litmus. The first urine passed tends to be a little more acid—averaging *p*H 5·4—but otherwise in the neonatal period the reaction of the urine is similar to that in later childhood.

Specific gravity.—The specific gravity of the urine is low in childhood, but is capable of wide and rapid variations according to the fluid intake. It is possible by promoting diuresis and later withholding fluids to produce a variation from 1002 to above 1035. In the first few days of life urine is normally dilute, with a specific gravity of 1012 (range 1008 to 1018) on the first day, rising a little and then falling to 1008 (range 1006 to 1011) on the seventh.

Formed elements.—Microscopically the urine of the newly-born child may show the presence of crystals of uric acid, squamous epithelial cells and even hyaline casts without any evidence of disease. Later, although the kidney does excrete red blood cells, leucocytes and casts, their numbers are so small that they are seldom seen on direct microscopy. In an older girl a non-catheter specimen may contain vaginal epithelium. A quantitative determination of the formed elements in urine was established by Addis, and his technique has been applied to children by Snoke and others. They have shown that in the twelve hours' night urine a healthy

child excretes on an average 80,000 red blood cells, 3,000 leucocytes and 1,000 casts; maximal figures reported by these authors for red cells and casts are 800,000 and 30,000 respectively. In the case of leucocytes, the number per c.mm. in a shaken, fresh specimen of urine can be determined in a counting chamber. Stansfeld and Webb have investigated the urine of healthy infants and children by this technique, and found that most healthy children have less than 10 leucocytes per c.mm.; figures above 100 are seldom found in health.

Frequency and control of micturition.—The normal infant commonly micturates within a few minutes of birth, but it is recognized that a healthy infant may pass no urine during the first twenty-four or forty-eight hours. Thereafter the frequency of micturition varies according to age and fluid intake, becoming less frequent as the infant grows. Engel, using an ingenious apparatus which signalled each emission of urine, found that a normal infant taking 25 ounces of food a day voided on an average twenty-five times in twenty-four hours. During sleep practically no urine is passed. During the third year it is passed every two or three hours, and may be retained eight or nine hours at night. Normally, control of the act is gained about the end of the second year, though the child does not become completely secure in this control until the sixth or seventh year. Due to the weak neuro-muscular control of the bladder in young children, urine is often passed as a result of the strain of crying. This combination of crying and passing urine may be misinterpreted as evidence of painful micturition.

Reactions of the kidney to general disease.—The physiological responses of the kidney to changes in other organs have already been noted, and it may be of advantage to review briefly the changes in pathological conditions. First may be mentioned circulatory changes. In congestive heart failure the rate of blood flow through the glomeruli and, consequently, the glomerular filtration are reduced; as a result the flow of filtrate through the tubules is diminished, giving longer time for absorption of water. Thus, the quantity of urine is diminished, while its concentration is increased. Owing to anoxæmia, the glomerular capillary permeability is increased, so that protein appears in the urine. The lowered glomerular filtration leads to lowered elimination of metabolites, and the blood urea may well rise to 100 mgm. per 100 c.cm. There is also sodium retention, an important factor in cardiac œdema. In severe shock, or following a large hæmorrhage, there is reflex constriction of the renal vessels, again lowering glomerular blood flow, with results similar to those just mentioned. In extreme cases there may be complete cessation of blood flow through the cortical glomeruli, leading to total anuria. As recovery ensues, the first urine passed contains protein, and perhaps red cells and casts, while occasionally the kidney changes may be irreversible, and death may ensue. In dehydration, again, glomerular filtration and urine output may fall below the level necessary for normal elimination of metabolites. The changes in the urine following electrolyte loss, acidosis and alkalosis have already been described.

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CLINICAL EXAMINATION

In most respects the method of examination is the same as that which is commonly used for adults. It should include palpation of the testes, bladder and kidneys. In females the vulva should be inspected, both for the detection of vulvo-vaginitis and for its exclusion as a possible source of pus cells when these have been found in the urine. Actual viewing of the act of micturition is helpful when valvular obstruction of the urethra is suspected, the weak and hesitant stream of urine in such cases being a valuable physical sign. Systemic examination will include inspection for œdema, examination of the optic fundi and estimation of the blood pressure. Collection and examination of the urine normally follows physical examination.

Method of collection.—For routine purposes this presents no difficulties in the older child. In the infant care should be taken to wash the external genitalia free from dusting powder; otherwise there may be confusion on microscopic examination. From a male infant the urine can be collected in a test-tube strapped to the penis, and from a female

infant by placing her on a padded bowl; rarely is it necessary to use a special glass or rubber device made to fit closely to the vulva. Failure to collect urine from infants is due usually to impatience or to lack of care. Difficulty arises only in the case of dehydrated female infants with diarrhœa, but even from these an unmixed specimen can usually be obtained shortly after giving 10 per cent. solution of cane sugar to promote diuresis. Specimens obtained in these ways are adequate for routine chemical and microscopical examination. For certain purposes it is necessary to collect and measure the volume of urine passed in twenty-four hours. When, for research purposes, an accurate determination of *p*H and of carbon dioxide tension is needed, the urine should be collected by catheter directly into a vessel under toluol. The precautions in obtaining specimens for bacteriological examination are described in the next chapter.

Urine testing.—The routine testing of the urine for reaction, specific gravity, and the presence of protein, glucose, bile pigments and other abnormal chemical constituents, being identical with that used in adults, needs no special consideration here. An estimation of the *p*H is often useful, and, for clinical purposes, the use of standard indicator test papers on a fresh specimen is adequate. Only rarely, or for research purposes, is accurate laboratory determination needed. Estimation of the chloride content is often of value, especially during treatment of dehydration, and the simple method of Fantus popularized by Marriott is sufficient for most occasions. To ten drops of urine in a wide test tube is added one drop of 20 per cent. solution of potassium chromate. A 2·9 per cent. solution of silver nitrate is then added drop by drop until the colour changes from yellow to brown. The number of drops added is approximately equal to the concentration of chloride in the urine expressed as grammes of sodium chloride per litre. It is most important that distilled water be used for preparation of the solutions and for cleaning out the test tube, that the same dropper be used for the urine and silver nitrate solution, and that it should be thoroughly rinsed with distilled water between these uses.

The detection of amino acids in the urine is performed most conveniently by the method of paper chromatography, but description of this technique would be out of place here.

Microscopic examination of the urine in the infant is essential; many incorrect diagnoses have been made owing to omission of this simple procedure. For routine purposes it is sufficient to place a large drop of urine from a fresh, shaken specimen on a clean slide, without a coverslip, and examine it under the low power of the microscope. Only if abnormal cellular constituents are found is it advisable to add a coverslip and carry out more detailed examination under the high power. A rough estimate of the numbers of formed elements can be made, an average of one cell per high power field representing approximately 250 to 500 cells per c.mm. Greater accuracy can be obtained by direct counting of cells from a fresh, shaken specimen in a white-cell counting chamber. The normal ranges have already been mentioned. As the numbers of the cells excreted

varies widely from specimen to specimen, it is important that, in any case of doubt, several examinations should be made. Thus, in a case of chronic urinary infection a few counts ranging round 10 cells per c.mm. may be followed by one of 200 per c.mm. The Addis technique for enumerating formed elements is particularly useful in detecting latent activity in nephritis, and the normal ranges have already been quoted. The examination is time-consuming and requires practice, so that its chief value is in research, but there are occasions in which it is of great help in prognosis. On the day of the test the child should have no food or fluid after midday until after completion of the test next morning. The bladder is emptied at 8 p.m. and the urine passed is discarded. Any urine passed during the night is retained, and added to that obtained on emptying the bladder again at 8 a.m. next day. The total volume of the night twelve hours is measured, the specimen is thoroughly mixed, and 10 c.cm. are thoroughly centifruged in a graduated centifruge tube. The upper 9·0 c.cm. are carefully pipetted off, and the deposit is thoroughly shaken in the remaining 1·0 c.cm. A drop of this fluid is then placed in a white cell counting chamber, and the numbers of red blood cells, leucocytes and casts per c.mm. estimated. The figure in each case, multiplied by 100 and again by the total volume in c.cm., will give the total number excreted in the night twelve hours. The reason for using the night twelve hours and for the dietary precautions is to ensure that the resultant specimen will be sufficiently concentrated to prevent lysis of formed elements.

Renal function tests.—The whole conception and scope of renal function tests has become considerably enlarged. The earlier tests, capable of detecting only gross deficiencies of the excretory functions of the kidneys, were of considerable value in assessing operative risks and of some value in prognosis, but were virtually useless in diagnosis. By looking on a full chemical analysis of the blood as an index of renal function, and by including the more recent clearance methods, more precise diagnosis as well as prognosis can be achieved by the use of tests of renal function.

The most simple test is based on the specific gravity of the urine; fluid is withheld after the mid-day meal, and the specific gravity of the first specimen passed next morning is measured. Following this fluids are pushed, and the specific gravity of a further specimen is estimated. In a healthy child the early morning specimen should have a specific gravity of 1020 or over, while that of the second should fall below 1008. A failure to reach these limits indicates impairment of the concentrating powers of the kidney, while in severe renal failure the specific gravity becomes fixed between the limits 1008 to 1012. This simple test, which can readily be performed in the home, is of help in diagnosing renal failure, and in the prognosis of chronic nephritis.

Routine laboratory estimates of blood chemistry afford valuable evidence of kidney disease and failure (for normal values see p. 132). The level of the blood urea is the most convenient guide to renal excretory powers, and any rise above normal levels indicates renal failure, though

not necessarily renal disease. Thus, temporary reduction of renal blood flow, as after severe hæmorrhage, will cause a rise in blood urea, and a similar phenomenon is seen in dehydration. In such cases the degree of the rise will be a pointer to the urgency of therapy. In chronic nephritis a steadily rising blood urea is of serious prognostic import. Estimations of other nitrogenous products, such as uric acid or of the total non-protein nitrogen can be interpreted similarly. Rises in plasma phosphate frequently occur in chronic renal disease, and their estimation helps in interpreting the clinical picture. Estimations of blood chloride and of alkali reserve, apart from being valuable in controlling treatment, are an essential part of the diagnosis of " nephrocalcinosis," which is characterized by a hyperchlorænic acidosis. Serum protein estimation, though not strictly a test of renal function, is a valuable diagnostic measure in œdematous patients.

The clearance tests, developed by Van Slyke, are the most sensitive tests of renal function. The basis of the tests is that, for substances like urea which are passively absorbed by the tubule cells, the rate of excretion of the substance is directly proportional to its plasma concentration, provided that the rate of formation of urine does not fall below a certain minimum. The proportionality can be expressed quantitatively by dividing the concentration of the substance in the urine by its concentration in the blood, and multiplying the result by the rate of excretion of urine in c.cm. per minute. The figure obtained, which can be regarded as the volume in c.cm. of blood from which the substance has been completely removed by the kidneys in one minute, is termed the clearance value for that substance. In the healthy adult, provided that the rate of excretion of urine is above 2 c.cm. per minute, the clearance value for urea is 75 c.cm. per minute, and this figure is termed the " maximal clearance value " for urea. If the output of urine falls below 2 c.cm. per minute the clearance value falls, being proportional to the square root of the volume passed per minute (minute volume). By simple arithmetic it can be referred to the clearance with a minute volume of 1 c.cm. ; this corrected figure is termed the " standard urea clearance " and is 54 c.cm. per minute for a normal adult. In the case of a child, corrections must be applied for the surface area of the body, which can be determined from tables if the child's height and weight be known. It is customary for the laboratory to apply all necessary corrections and supply the result as " maximal " or " standard " urea clearance, depending on circumstances, corrected to normal adult surface area—so that the result can be compared with the normal averages of 75 and 54 c.cm. per minute respectively—or simply to give the result as a percentage of normal average, the normal range being between 75 and 125 per cent. of the average.

In carrying out the test the bladder is emptied and the urine discarded. After accurately timed intervals each of about an hour the bladder is emptied on two further occasions, and the two specimens measured and sent to the laboratory, together with specimens of blood for urea estimation collected at approximately the mid-points of the two intervals. If

the minute volume of urine is low, the test can be made more accurate by raising the output of urine by the administration of urea, 1 gramme per year of age, at the onset of the test. The data to be supplied to the laboratory, apart from those of identification, must include the height and weight of the child, the exact time intervals and the volumes of urine passed.

Certain other clearance tests, used almost entirely for research purposes, may be mentioned briefly, chiefly to facilitate understanding of the relevant literature. Certain substances, notably inulin, are filtered by the glomeruli but undergo no absorption in the tubules. The volume of plasma cleared of such a substance in each minute is therefore equal to the volume of plasma filtered by the glomeruli in each minute. Inulin clearance tests are thus used to measure glomerular filtration rates. Diodrast is a substance excreted both by glomeruli and tubules, and, provided that the plasma level is not too high, diodrast is completely removed from the blood during one passage through the kidney. An estimate of diodrast clearance with low blood level, therefore, gives a direct measure or renal blood flow. Homer Smith has developed further tests using " Tm " or " maximal transfer " estimations. In this terminology, the maximum quantity of glucose, expressed in mgm. per minute and estimated by suitable techniques, which can be excreted by the glomeruli and reabsorbed by the tubules is termed the " glucose Tm." Similarly the maximum amount of diodrast, again expressed in mgm. per minute, which can be excreted by the kidneys, the blood level being suitably raised for the purpose, is termed the " diodrast Tm." By suitably integrating the glucose and diodrast Tm figures with the inulin clearance it is possible to form estimates of the functional masses of intact nephrons, glomeruli and tubules.

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THE USE OF DRUGS IN KIDNEY DISEASE

Diuretics.—Of the many drugs having diuretic actions only a few of proved worth will be mentioned. The type of drug will vary with the particular purpose for which diuresis is desired, and it must be stressed that only rarely are diuretics indicated in kidney disease; in acute nephritis and most varieties of anuria they are absolutely contra-indicated.

When the purpose of the diuretic is to eliminate toxins, or to achieve

an abundant flow of dilute urine, as in urinary tract infections and during the administration of sulphonamides, the most valuable diuretic is water, either by mouth—plain, or flavoured with orange, barley etc.—or intravenously as 5 per cent. dextrose solution, when the oral route is impracticable. The quantity needed will vary with the age of the child, but as a guide a figure of four pints per day for a five-year-old may be quoted.

Drugs acting osmotically in the renal tubules are of value in cardiac and nephrotic œdema, and a useful example is urea, given in a dosage of from 10 to 20 grammes with complete safety, provided there is no gross nitrogen retention. Dextrose given intravenously in a dosage of from 10 to 40 c.cm. of a 50 per cent. solution also acts osmotically; its chief value is in encouraging urine flow after reflex anuria, and to produce cerebral dehydration. Sucrose, though more efficient than dextrose for the purpose, is not without risk, and should not be used.

The mercurial diuretics are not fully understood, but there is evidence that they act on the tubules and hinder absorption of water. Although their indications for use in childhood are few, they can be strikingly effective in appropriate conditions. Cardiac œdema is the chief indication. Occasionally they may be used as a measure of desperation in an older child with nephrosis, but the risk of sudden collapse or even death must be recognized, and a mercurial diuretic should not be used in nephrosis in infancy. Nephritis or any form of renal failure is a complete contra-indication. Mersalyl, the officially recognized member of the group, is given by intramuscular injection, a dose of from $\frac{1}{2}$ to 1 c.cm. being suitable for a child of five years, and double this dose for a fourteen-year-old. The injections may be repeated on alternate days several times. The administration of an acidifying drug, in itself a weak diuretic seldom used alone, can greatly potentiate the action of mersalyl, and to this end it is customary to give ammonium chloride for forty-eight hours before each injection of mersalyl, the dosage being $\frac{1}{2}$ c.cm. ($8\frac{1}{2}$ minims) four-hourly to a five-year-old, administered in the mixture described in the National Formulary.

Anti-diuretics.—Apart from experimental and diagnostic purposes the only indication for the use of anti-diuretics is diabetes insipidus, and the only effective anti-diuretic is the naturally occurring hormone of the pituitary gland. This can be administered hypodermically in the form of pitressin tannate in dosage of 0·1 to 0·5 c.cm. per day, the dosage being adjusted in accordance with urinary output.

Acidifying drugs.—The two commonly used acidifying drugs are acid sodium phosphate and ammonium chloride. The former, on excretion, lowers the *p*H of the urine. In the latter case the ammonium ions become converted to urea in the body, leaving an excess of chloride ions for excretion, causing a tendency to systemic acidosis and an acid urine. The dosages can be calculated on the usual basis from the adult doses of 15 to 30 grains of acid sodium phosphate and 30 grains of ammonium chloride four-hourly, but must be adjusted by checking the reaction of fresh specimens of urine, being increased or decreased until the desired *p*H is reached.

Alkalinizing drugs.—Sodium bicarbonate is an effective drug for alkalinization of the urine, as is sodium citrate, which becomes converted in the body to sodium bicarbonate. The dosage must be adjusted in each patient until each specimen of urine tested immediately after being passed is alkaline to litmus, the initial dosage being equivalent to an adult dose of 30 grains four-hourly in each case. For prolonged administration the citric acid—sodium citrate mixture of Albright and Shohl is valuable ; as it does not alter the *p*H of the intestinal contents it does not interfere with the absorption of calcium and phosphorus. The mixture consists of 60 grammes of citric acid and 100 grammes of sodium citrate dissolved in 1 litre of water. For an infant of a few months a dosage of 6 grammes of sodium citrate daily in this mixture may be given initially.

Urinary antiseptics.—The introduction of the newer antibiotics has rendered obsolete many of the older urinary antiseptics, but has also created new problems. Rapid changes are occurring in this field of therapy, and the views here expressed may well require modification in the near future.

At present the drugs of the greatest value in urinary infections in general, and which are successful in most acute infections, are those of the sulphonamide group, and the member of this group favoured by the writers is sulphamezathine (sulphadimidine B.P.). As the substance of the kidney is so often involved in addition to the lining of the urinary passages, dosage should be such as to produce an adequate blood level rather than merely a bacteriostatic level in the urine. The dosage is, therefore, identical to that given for an infection of moderate severity elsewhere in the body, *e.g.* an initial 2 grammes followed by 1 gramme six-hourly for a five-year-old child. This dosage should be maintained for at least five days ; if the response in the urine is not rapid it is advisable to continue administration for ten days. Except where the urine is already alkaline, concomitant administration of sodium bicarbonate to alkalinize the urine is a useful adjunct.

Only when sulphonamide has failed should the antibiotics be considered, and preferably only after the nature and the sensitivity of the infecting organism has been established. Penicillin is not often indicated, but is the antibiotic of choice in the rare staphylococcal urinary infections. Streptomycin held great promise owing to its effect on organisms of the coliform group, so frequently the causal agents in the urinary infections, but the rapid emergence of resistant strains has greatly limited its value in practice. Chloramphenicol and aureomycin should be used in urinary infections when there is an adequate bacteriological indication.

In chronic infections both sulphonamides and the antibiotics have proved disappointing. Too often an initial success is followed by a relapse, and in this the organisms are found to have become resistant. Change to another antibiotic may succeed, and is worth a trial, but may well be followed by further relapse. It is in such circumstances, and when no remediable surgical cause for recurrence can be found, that there remains a place for the older antiseptics—hexamine, hexylresorcinol and mandelic acid. Though these are seldom curative in the circumstances mentioned,

they do at least control the infection for long periods, and drug resistance does not arise, so that these drugs can be given as effectively in a relapse as in a first infection. The writers have found the combination of hexamine and mandelic acid in "Mandelamine" effective, easy to administer and free from disadvantages. The drug is administered in enteric-coated tablets, each containing 0·25 gramme of hexamine mandelate ($3\frac{3}{4}$ grains), and the adult dosage is 3 to 4 tablets three times daily; dosage in childhood is proportionate, and an infant can be given one tablet twice daily.

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Albuminuria

Albuminuria is an important feature of many diseases of the kidney, and no useful purpose would be served by attempting a comprehensive catalogue of these conditions. Its occurrence as a transient phenomenon in healthy neonates has already been mentioned, and it is a common accompaniment of many infective and febrile conditions in infancy and childhood. In addition, it may occur as a persistent or recurring condition over long periods in apparently healthy individuals. MacLean examined 60,000 soldiers and found that 5 per cent. had albuminuria for which no cause could be found. No figures are available for such a large number of children, but the incidence of benign albuminuria is probably higher than 5 per cent. Dukes found 157 cases among 1,000 schoolboys between the ages of thirteen and fifteen years, and Bashford 58 cases in another group of 1,000 boys. Lauener examined 5,000 school-children and found albuminuria in 6 per cent. of those aged six to seven years; 27 per cent. aged ten to eleven years; 38 per cent. aged fifteen to sixteen years. Some further consideration of this benign or "functional" albuminuria, so common in later childhood, is required.

Functional, orthostatic, postural or cyclical albuminuria.—Extensive investigations in the earlier part of the present century established the harmlessness of this condition, and showed that it was in no way connected with organic disease of the kidneys. The chief characteristics have been variously pointed out by Pavy, Stirling, Haubner, Jehle and others: (1) the albuminuria is intermittent; (2) it is absent or reduced to the merest trace when the patient is lying down and reappears when the erect posture is assumed; (3) in more than 50 per cent. of the cases lordosis accentuates the condition and may be the actual cause of it. Most cases occur between the ages of five and sixteen years, with an increasing frequency up to puberty, after which the incidence decreases quite rapidly. It is equally common in both sexes and may affect more than one member of the family. It is probably related to the albuminuria following cold baths or severe muscular exertion, and it is generally believed that the albuminuria is the result of disturbances in the renal circulation brought about by vaso-motor influences.

Orthostatic albuminuria is usually discovered accidentally in routine examination without there being any symptoms to draw attention to the kidneys. In diagnosis the first essential is the exclusion of nephritis by the history, absence of œdema, absence of red blood cells from the urine and by the use of renal function tests. Other general disease capable of causing albuminuria should also be excluded. The albuminuria should be shown to be intermittent, so that one specimen or other of urine during the day—usually the early morning specimen—should be free or almost free from it. Standing erect or in a position of lordosis should readily provoke an increase in the albumin. It should be borne in mind, however, that in some cases of nephritis the albuminuria may vary from hour to hour and be affected by posture. Diuresis and alkalinization of the urine should decrease the albumin.

As the condition is harmless no treatment is needed, and anxious parents can be reassured.

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Hæmaturia

The presence of blood in the urine being merely a symptom of some local or general disease demands careful consideration. It must be distinguished from hæmoglobinuria in which blood pigment (with perhaps an occasional red cell) is present, and for this and other reasons a microscopic examination of the urine is always necessary. The following division may be made of the conditions under which hæmaturia occurs in children :

(1) *General diseases.*—Bleeding from the kidneys or bladder occurs in the blood disorders, especially anaphylactoid purpura and thrombocytopenic purpura, severe acute infective illnesses and infantile scurvy. Hæmaturia, microscopic or macroscopic, is a frequent symptom of subacute bacterial endocarditis and of polyarteritis nodosa. The " hæmorrhagic disease of the new-born " usually results in bleeding from the bowel or vagina, but in a few cases from the kidney also.

(2) *Renal causes.*—Amongst these, the commonest is acute glomerular nephritis, in some cases of which there may be only slight constitutional symptoms. When the cause of renal bleeding cannot be determined, it is a safe clinical rule to look upon the case as being one of glomerular nephritis, without constitutional symptoms, until it has been disproved. It is better to adopt this attitude than to be lulled into a sense of false security in making a diagnosis of " renal epistaxis." Rare causes are

tuberculosis, stone, parasite, injury, tumour and a capillary nævus of a renal papilla. It is surprising, however, how frequently blood is absent from the urine with new growths. In new-born infants it may be due to uric-acid infarcts, or the passage of calcium oxalate crystals, and occasionally to vascular disturbances in the kidney, especially venous thromboses, which are prone to accompany severe infection with dehydration. Damage to the kidneys by the acetyl derivatives of the sulphonamide drugs, notably sulphadiazine and sulphamerazine, is an important cause. Hæmaturia due to toxic agents such as cantharides and carbolic acid is rare.

(3) *Affections of the urinary tract.*—Primary disease of the bladder and ureters is an extremely rare cause of hæmaturia in children, only a few cases of new growth of the bladder having been reported and most of these under the age of five. Bilharziasis is a common cause in countries where an infection is possible, but unknown otherwise. Bleeding may accompany cystitis, and the authors have seen one peculiar case in a girl of defective intelligence who was found to have a foreign body in the bladder which produced cystitis and intermittent hæmaturia.

Rarely patients may be seen who have more or less constant hæmaturia without any discoverable cause, but the failure to find a cause must not be admitted until complete examination, including cystoscopy and ureteral catheterization, has been undertaken. Guthrie and also Aitken have described a familial form of hæmaturia, the pathological basis of which was not determined. A rare cause noted by Still is bleeding from the kidney during paroxysmal whooping-cough; and the authors have seen hæmaturia in a case of lymphadenoma which accompanied the Pel-Ebstein febrile periods and disappeared in the afebrile periods.

The treatment of hæmaturia is the treatment of the cause upon which it depends.

Hæmoglobinuria

The excretion in the urine of blood pigment, whether this be hæmoglobin or one of its derivatives, is referred to as hæmoglobinuria. The urine is brownish-red or almost black in colour, and the condition must be distinguished from hæmaturia and from coloration of the urine by other pigments. Microscopy readily makes the distinction from hæmaturia, even though a few red cells may be present in true hæmoglobinuria. Some children excrete unchanged in their urine the red pigment of beetroot, but the colour of the urine is a brighter red than that of hæmoglobinuria, and reassurance of the anxious parent is usually easy. Urine may be stained pink by the dyes used in boiled sweets, but a characteristic greenish fluorescence makes recognition simple. Again, the staining pink of an infant's napkins by urates may alarm a mother, but should not deceive her medical attendant. Porphyrins (see p. 353) cause the urine to be port-wine colour, while in alkaptonuria (see p. 356) the urine is of normal colour when passed but darkens on standing. A preliminary guaiacum test followed by spectroscopy of the urine should establish the diagnosis of hæmoglobinuria.

The pigments in hæmoglobinuria consist usually of methæmoglobin

and hæmoglobin, occasionally of sulphhæmoglobin. The condition, which is extremely rare in childhood, is the result of rapid intravascular hæmolysis, and is seen after incompatible blood transfusions. It occurs also in acute hæmolytic anæmias of the Lederer type, in which an antigen-antibody reaction is probably the cause. Toxic damage to the red cells, leading to hæmolysis and hæmoglobinuria, is seen in poisoning from such agents as potassium chlorate, naphthol, hydrogen sulphide and lewisite; cases have been reported after the use of santonin and extract of male fern. It may occur in acute infective illnesses, and Winckel's disease, an epidemic form in newly-born infants associated with icterus and cyanosis, is probably a manifestation of neonatal sepsis. In addition to these types, which occur in single episodes, there is a recurrent type, known as paroxysmal hæmoglobinuria, which will be described separately.

The chief danger of hæmoglobinuria lies in the renal damage which may result, and which may produce anuria and death. It was at one time thought that the anuria was the result of obstruction of the renal tubules by precipitation of the hæmoglobin derivatives by the acid urine, and treatment by alkalis was advocated, but it is now recognized that the mechanism is more complex, and that the renal lesions come under the heading of "lower nephron nephrosis"; the nature and treatment of this will be discussed more fully later. In cases of hæmoglobinuria due to incompatible blood transfusion, the administration of a further, but compatible, transfusion is of value.

Paroxysmal hæmoglobinuria is a peculiar and well-defined condition in which there are intermittent bouts of hæmoglobinuria accompanied by backache, malaise and frequently by the Raynaud syndrome. In most cases the attacks are provoked by exposure to cold, and occur at irregular intervals. The patients themselves are usually the first to make the observation that urinary changes are symptomatic of the attack. The hæmoglobinuria rarely persists for more than one or two days, often only a few hours. The disease is not fatal, and the prognosis depends on the underlying cause; in children this is almost invariably syphilis. In 59 cases recorded by Browning and Watson, 90 per cent. had a positive Wassermann reaction. It appears that the blood of certain syphilitic patients contains an autohæmolysin, which becomes active at low temperatures. The view that this hæmolysin can give rise to a positive Wassermann reaction is now discredited, and Nabarro strongly upholds a syphilitic origin for these cases, and attests to the value of anti-syphilitic treatment. Apart from the treatment directed against syphilis, the only measures needed are protection from cold, and treatment of the anæmia resulting from the blood loss, either by iron or, in more severe cases, by blood transfusion.

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Pyuria and bacteruria

In general the presence of pus cells in the urine in significant numbers, as previously defined, indicates the existence of an infection of the urinary tract calling for treatment, and the problems of urinary tract infections will be considered later. Severe dehydration in an infant, however, may be accompanied by the presence of a few pus cells in the urine without manifest urinary infection, and in some cases of acute appendicitis a mild pyuria may occur. It is important, also, to ensure that pus cells found in urine collected routinely have not found their way from the vulva of a female or preputial space of a male; in cases of doubt the collection of a specimen by catheter is necessary.

The invasion of the urinary tract by micro-organisms does not necessarily provoke pyuria. Schwartz found that gram-negative bacilli are present in the urine of the majority of children with acute gastro-intestinal disease, and in 21 per cent. the number was sufficient to constitute a bacilluria. Furthermore, there is no doubt that one of the functions of the kidney is the excretion of micro-organisms, and that in septicæmic conditions, scarlatina, typhoid fever and other diseases the causative organism may find its way into the urine without setting up nephritis or pyelitis. Treatment of the urinary tract is not indicated for bacilluria in the absence of pyuria.

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Aminoaciduria

Amino acids are normally present in the urine in small amounts, commonly between 10 and 30 mgm. per 100 c.cm. expressed as amino nitrogen. When they are excreted in abnormally large amounts the term aminoaciduria can be applied. It has long been known that aminoaciduria accompanies severe destruction of liver parenchyma, and the older clinicians advised microscopic examination of the urine for crystals of leucine and tyrosine as an aid to the diagnosis of acute hepatic necrosis. More refined methods of examination reveal the excess of amino acids in the urine in lesser degrees of liver damage, as in cirrhosis. In Kinnier Wilson's disease—hepato-lenticular degeneration—aminoaciduria exists, and is now thought to precede the cirrhosis and to be a manifestation of an underlying metabolic disorder. One of the rare but well recognized inborn errors of metabolism is that of cystinuria. In this condition many other amino acids, in addition to cystine, are excreted in excess in the urine; the insolubility of the cystine in acid urine, however, results in calculus formation, the presenting symptom of the disorder, which has led to attention being concentrated on this one amino acid with neglect of the others. The disorder is first recognized usually in later childhood or adult life, but we have observed a case in an infant of eleven months, in whom the presenting symptom was anuria associated with cystine calculi in the ureters.

Cystinosis, or Lignac's disease, is a condition of infancy in which excretion of amino acids in the urine is associated with deposition of cystine crystals in tissues throughout the body, including the cornea, where they can be recognized by use of the slit-lamp. Death from infection commonly occurs in infancy. In the de Toni-Fanconi syndrome, aminoaciduria is associated with glycosuria and intractable rickets (see later). There has been considerable discussion on the relationship between cystinuria, cystinosis (Lignac's disease) and the de Toni-Fanconi syndrome, and Bickel argues that Lignac's disease and the de Toni-Fanconi syndrome are essentially the same disorder, and should be clearly differentiated from cystinuria.

Occasionally crystals of amino acids, especially cystine, may be found on direct microscopy of urine, but the recognition of aminoaciduria is most readily and certainly accomplished by paper chromatography. In all cases of aminoaciduria alkalinization of the urine to facilitate excretion of cystine is advisable.

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Anuria

Anuria, or suppression of urine, in which no urine reaches the bladder owing to glomerular failure or obstruction in the tubules or ureters, must be distinguished from retention where the failure is in emptying of the bladder. The distinction is usually readily made by palpation of the bladder, but occasionally the passage of a catheter may be necessary.

It should be remembered that anuria may be physiological in the first forty-eight, or even seventy-two, hours of life ; we have seen an infant with a bruised and swollen prepuce, the result of an instrumental assault in an effort to relieve an imaginary obstruction. In severe dehydration in infancy there may be temporary anuria, and the failure of an infant with pyloric stenosis to wet his napkins is evidence of the seriousness of his plight. Bilateral ureteral obstruction will naturally lead to anuria, but in some cases urine may be suppressed when only one ureter is obstructed by a stone ; in these cases it is presumed that a reflex nervous mechanism causes restriction of the blood supply to the glomeruli of the opposite kidney. Anuria is a well-recognized complication of sulphonamide therapy, and it seems likely that two different mechanisms may be involved. One, which is seen especially with sulphapyridine, sulphathiazole, sulphadiazine and sulphamerazine and where the urine is acid and concentrated, is purely mechanical, due to obstruction of the renal tubules or ureters by masses of crystals of the acetyl derivate of the sulphonamide. The second mechanism appears to be a sensitivity reaction, producing lesions in the kidney similar to those seen in the anuria associated with incompatible blood transfusions, crush syndrome and blackwater fever. These changes will be discussed later under the heading of " lower nephron

nephrosis." Finally, anuria may occur in the early stages of acute nephritis.

The treatment of anuria will depend on the cause. Dehydration should be corrected and obstruction relieved. Sulphonamide anuria of the mechanical type should be prevented, partly by using whenever possible a sulphonamide, such as sulphamezathine, less prone to crystal precipitation, and partly by ensuring an adequate flow of alkaline urine. In a dehydrated infant sulphonamide should not be given until it is known that the infant is passing urine in adequate amounts. If, in a patient receiving sulphonamide, anuria follows a period of hæmaturia or oliguria with acid urine containing crystals, it is probable that the obstruction is mechanical in origin. Sulphonamide administration should be stopped, and the patient should be given alkalis and abundant fluids by mouth, or intravenously if necessary. If this fails to restore urine flow within twenty-four hours, cystoscopy and ureteric catheterization should be performed, and the renal pelves irrigated until no further crystals are returned. No way, other than removal of the cause, is known of affecting favourably the renal lesions of the lower nephron nephrosis, and in many cases these are irreversible, and lead irrevocably to death. Spontaneous recovery of the kidney can, however, occur, and treatment of cases of anuria from this cause should be aimed solely at keeping the child alive long enough for this spontaneous renal recovery to take place. It now seems clear that the older method of treatment by forcing fluids killed more patients than it cured, and modern treatment aims at keeping the volume and chemistry of the body fluids as close to normal as possible. This can be achieved by the use of an artificial kidney or by peritoneal dialysis ; but the former requires highly specialized apparatus, and both are extremely dangerous in the absence of perfect biochemical control. Results, which if not equal are at least almost so, can be obtained much more simply. Sufficient fluid is given to replace that lost in vomitus and invisibly through the lungs and skin, and glucose is given in sufficient quantities for energy requirements so as to avoid unnecessary metabolism of body protein, and electrolytes to replace any loss in vomitus. Pratt advises that the child should be weighed daily, and should have daily estimates of the plasma sodium, chloride and bicarbonate ; from these figures the daily requirements of water and electrolytes can be calculated, and the patient is given these quantities either by mouth or intravenously, together with 100 to 200 grammes of glucose. Bull recommends a regime which is easier of achievement. Arguing that the daily insensible water loss averages 1,000 c.cm. for an adult, and that other water and electrolyte loss is almost entirely by vomiting, he recommends that an adult be given daily, by plastic stomach tube, an emulsion of 400 gm. glucose and 100 gm. peanut oil with sufficient acacia to enable emulsification in water to 1,000 c.cm., and that any vomitus is filtered and returned by the tube.

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Uræmia

Uræmia is the symptom complex produced by chemical changes in the body fluids in renal failure, these symptoms being differentiated from those due to cerebral vascular changes associated with the hypertension which so often accompanies renal disease. Of the many chemical changes in uræmia the most obvious is the accumulation in the blood of nitrogenous end products; the largest of these, urea, though probably blameless in the symptomatology of uræmia, forms a useful yardstick for measurements and diagnosis. Retained organic acids and phenols probably account for drowsiness, coma, vomiting and acidosis, the last manifesting itself by air-hunger. Dehydration results in those cases in which polyuria is a feature of the kidney disease, and is aggravated by vomiting. In chronic cases, phosphate retention causes loss of calcium by the bowel; the lowered calcium can lead to tetany, and the disturbed calcium-phosphorus ratio to rickets and dwarfism.

Depending on the nature and severity of the renal disease, uræmia may be seen in acute and chronic forms. The acute form—previously known as "urinæmia" or "urinary poisoning"—is seen when anuria, as occurring with bilateral cortical necrosis, bilateral ureteral obstruction and the lower nephron nephrosis already mentioned, is complete and persists for several days. Its earliest symptoms are usually quite undramatic, and even with complete suppression of urine they may not be evident for four or five days. The patient feels tired and weak; vomiting follows, and drowsiness passes into coma. Death follows within about ten days of onset if the urine flow does not become re-established.

In its more insidious and prolonged form uræmia is seen typically in the slowly progressive cases of chronic glomerular nephritis and is the common terminal state in "renal dwarfs." The first significant change is the appearance of lassitude, muscular weakness and loss of appetite. The breath becomes foul, the tongue coated, and stomatitis is often present. The skin becomes sallow and there is often true anæmia. The loss of appetite becomes an obstinate anorexia, and at this stage vomiting appears, to remain one of the most striking symptoms. The vomit may be large in quantity and watery, or there may be only continuous retching. Uræmic patients are prone to develop ulcerative or "diphtheritic" colitis, which shows itself by abdominal colic and the passage of loose or blood-stained stools. Another important feature is a sub-normal temperature, which may be raised but little above the normal level of health even in the presence of septicæmic complications. Occasionally a pericarditis ushers in the end, but the terminal stage is usually one of quiet coma.

To this picture of uræmia must be added two further groups of symptoms: (*a*) the peripheral muscular twitchings and positive Chvostek sign of hypo-calcæmia; as uræmia progresses the blood calcium level falls, so these symptoms are rarely absent, and in some cases, in which the course of the illness is severe and prolonged, attacks of frank tetany with carpopedal spasm arise; (*b*) the hyperpnœa of acidosis, which Rose Bradford describes as "hissing dyspnœa" of uræmia. Finally, both the dwarfism

and rickets of renal dwarfism can well be looked upon as manifestations of uræmia.

The progress of symptoms varies according to the chronicity of the disease. In some cases of slowly advancing chronic glomerular nephritis there may be for months only some anorexia, nausea, anæmia and muscular weakness with intermittent muscular cramps denoting hypocalcæmia. In other cases—frequently seen with renal dwarfs—it may run an intermittent or relapsing course, reaching stages of uræmic vomiting or even tetany, only to improve again as the renal function is temporarily re-established.

When uræmia remains uncomplicated, in the absence of raised blood pressure, there are no retinal changes, little or no headache, and no eclamptic symptoms.

The diagnosis of uræmia can usually be made from a simple clinical examination of the patient, but any doubt is readily set aside by seeking the confirmation of a blood urea estimation.

The treatment of acute uræmia is that of anuria, already described. In the chronic uræmia of progressive renal disease the simple duty of the doctor is to make his patient as comfortable as possible, treating symptoms as they arise, and avoiding measures which increase his misery, however logical they may appear biochemically.

The cerebral symptoms of arterial hypertension are seen most typically in cases of hypertension (essential hypertension) with normal renal function, but they are apt to arise in various forms and stages of nephritis accompanied by high blood pressure (renal hypertension), particularly at the onset of acute nephritis when the blood pressure is suddenly raised, and again in chronic glomerular nephritis with steadily rising blood pressure. The symptoms can be attributed to the occurrence of temporary cerebral anæmia from spasm of the cerebral arterioles. According to the area of the brain so affected they vary in degree and character. The most striking symptom is a major epileptiform fit, a true eclamptic seizure with generalized convulsions. This is the fit of "hypertensive encephalopathy" of Fishberg. Lesser degrees of the syndrome are transient hemiplegia, monoplegia, amaurosis, attacks of vertigo and headaches. Even in the cases of non-renal hypertension the attacks may be followed or accompanied by albuminuria. It is therefore readily seen how easy it is to confuse these states with uræmia. It is in the hypertensive state, whether it be renal or non-renal in origin, that "renal retinitis" arises. This takes the form of the characteristic flame-shaped hæmorrhages, white patches and glistening vessels.

Complete bed rest is the basis of treatment of these symptoms. In addition, a rectal injection of 5 ounces of 25 per cent. solution of magnesium sulphate may be given to reduce cerebral œdema, and soluble phenobarbitone may be given intramuscularly in a dosage of 3 grains to an older child having convulsions.

In general it may be taken that uræmia and hypertensive cerebral disorders are less common in children than in adults, but whereas in adults they are often complicated by other factors, it is in children that

the opportunity may occur of studying their manifestations in uncomplicated forms. This gives the subject a special scientific importance in pædiatrics.

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Renal venous thrombosis

In infancy and childhood, as in adult life, various forms of circulatory disorder may occur in the kidney, producing conditions such as infarction and cortical necrosis, but one condition, peculiar to infancy and needing special comment, is that of intra-renal venous thrombosis. This occurs especially in severely dehydrated infants, often those suffering from gastro-enteritis. The symptoms are often masked by those of the primary condition, so that most reports are of autopsy findings, unsuspected during life. Usually the condition is bilateral and incompatible with life, but if one kidney only is affected the infant may survive, and the renal damage may well lead to hypertension ; herein lies the importance of diagnosis. The affected kidney is swollen and dark red in colour ; on section it is seen to be the seat of hæmorrhagic infarction, hæmorrhage being most marked in the boundary zone. Histological examination shows thrombosis in the small radicles of the renal vein, sometimes extending into the main vein. The chief recognizable symptoms are hæmaturia and the presence of a lump in the flank ; other symptoms, such as a fall in the output of urine and evidence of renal failure, are masked by the original illness and dehydration.

We have seen an infant of eight weeks, who had been drowsy and irritable from birth, and who had begun to vomit on the previous evening. He was dehydrated and ill, and a large mass was palpable in the right loin. Albumin was present in the urine, and the blood urea was 230 mgm. per 100 c.cm. With intravenous fluids the infant improved and the blood urea fell to 60 mgm. per 100 c.cm. A week later there was hæmaturia, and the blood pressure rose to 145/80. Four days later a right nephrectomy was undertaken, the kidney showing the appearance already described. The infant made a rapid and complete recovery.

Renal venous thrombosis should be considered whenever hæmaturia occurs in a dehydrated infant, especially if the kidney becomes readily palpable on one or both sides ; if only one kidney feels enlarged, nephrectomy is indicated, dehydration having first been corrected.

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Bright's disease

It is commonplace to refer to the difficulty of finding for the various forms of Bright's disease a classification which satisfies clinicians and pathologists; it is difficult even to define what is meant by "Bright's disease" and "nephritis." The reasons for these difficulties are not far to seek. In the first place, it is now clear that widely differing ætiological agents may lead to almost identical pathological changes in the kidney; thus the pathological changes in the kidney resulting from sulphonamide poisoning and mis-matched blood transfusions may be almost identical, and it may be extremely difficult to distinguish the late results of the antigen-antibody reaction of acute nephritis from those of chronic suppuration and of simple vascular occlusion. On the other hand, the same agent, under different conditions, may produce widely differing changes. Finally, the functional disturbances, on which symptoms depend, are not always closely correlated with the histological changes in the kidney, and may depend considerably upon events occurring outside the kidney. Thus, it is possible to prepare a relatively simple clinical classification, having no reference to pathology, or a purely pathological arrangement of not too great complexity; but a classification under which every instance of Bright's disease can be positively identified in relation to ætiology, pathological anatomy and histology, and clinical symptoms is as yet impracticable, if not impossible of achievement. For a full description of the problems which underlie the search for a satisfactory terminology, the reader is recommended to consult the classical work of Volhard and Fahr, Fishberg's excellent book, the Medical Research Council reports of Gray and Dorothy Russell, and the more recent review by Ellis, whose nomenclature has been so widely accepted.

It should always be borne in mind that classification is not an end in itself, but a means to an end; the end, in the present context, is to enable the reader to recognize such cases of Bright's disease as he is likely to meet sufficiently clearly to advise reasonably on prognosis and management. It is, therefore, legitimate to adopt simple classifications, recognizing frankly that the less common examples of Bright's disease will not readily fit into these classifications; and to use separate classifications for discussing the pathology and the clinical manifestations, provided always that these classifications can be correlated with each other and with the nomenclature of other writers.

The pathology and nature of Bright's disease can be discussed under the following headings:

(*A*) *Nephritis*

1. Diffuse glomerular nephritis (*a*) acute (*b*) subacute (*c*) chronic.
2. Focal embolic nephritis.
3. Chronic pyelonephritis.

(*B*) *Nephrosis*

1. Larval nephrosis.
2. Necrotising nephrosis.
3. Lipoid nephrosis.

4. Amyloid nephrosis.
5. Lower nephron nephrosis.

(*C*) *Nephrosclerosis*
(*D*) *Congenital hypoplastic kidney*
(*E*) *Miscellaneous* (*a*) Ellis type II nephritis.
(*b*) Fanconi syndrome.
(*c*) Nephrocalcinosis.

For clinical description the following headings are proposed :

(*A*) *Acute nephritis*
(*B*) *Chronic œdematous Bright's disease*
(*C*) *Chronic Bright's disease with urœmia and hypertension*
(*D*) *Renal dwarfism and rickets*
(*E*) *Lower nephron nephrosis*
(*F*) *Nephrocalcinosis*

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Nature of Bright's Disease

Nephritis

(1) *Diffuse glomerular nephritis.*—The close relationship between diseases of the kidney and of small blood vessels has already been mentioned, and it is widely believed that acute diffuse glomerular nephritis is part of a generalized reaction of small vessels throughout the body to an antigen-antibody reaction, the antigen commonly concerned being derived from a hæmolytic streptococcal infection. The reaction occurs from seven to twenty-one days after infection, and Kellett has shown that it is accompanied by virtual disappearance of complement from the blood. The systemic vascular damage may lead to œdema, myocardial failure, hypertension and cerebral vascular reactions. In the kidney, the glomeruli are strikingly affected. The first microscopic change is in the endothelial cells lining the glomerular capillaries, which swell and proliferate to produce ischæmia of the glomeruli, as was clearly shown by Dunn and MacNee. Secondary degenerative changes occur in the cells lining the tubules, dependent for their blood supply on the glomeruli, and protein and blood cells are present in the Bowman's capsules and tubules. It is clear that complete resolution can, and in the majority of cases does, follow. This variety of Bright's disease is commonly referred to simply as acute nephritis, and by Ellis it has been named type I nephritis. In earlier classifications it was customary to consider " acute focal nephritis " as an entity separate from acute diffuse glomerular nephritis. The criteria of distinction were that, in the focal form, the hæmaturia occurred during the course of an acute infective illness and not after a latent period,

there was no rise in the blood pressure or alteration in blood chemistry, and complete recovery was the rule. Illingworth has shown that, in a series of cases of acute nephritis, it is impossible to separate the two types by means of these criteria, and considers that acute focal nephritis does not constitute a distinct clinical entity.

In certain cases of acute nephritis the lesions progress to the subacute and chronic forms. In the subacute form—also known as one form of "large pale kidney" or "chronic parenchymatous nephritis"—the glomerular changes have progressed, with proliferation of the epithelium, swelling of the tufts and the formation of epithelial crescents. The tubular cells are swollen and show degenerative changes.

In the chronic form, the damage to the glomeruli has passed in many cases to scarring and atrophy, and the associated tubules also are atrophic. Surviving nephrons are hypertrophied, and the renal architecture is grossly disorganized. Partial renal anoxæmia has led to hypertension, with secondary arteriolar thickening and Ellis maintains that the ultimate renal changes are due in large part to these vascular effects of hypertension rather than to the initial injury. The type of kidney change described was in older classifications spoken of as "small white kidney," "secondarily contracted kidney" and formed one variety of "chronic interstitial nephritis."

(2) *Focal embolic nephritis* (Löhlein), or multiple glomerular embolization (Fishberg) is a condition peculiar to subacute bacterial endocarditis, in which there is coagulation necrosis of varying numbers of glomeruli, due to the haphazard deposit of minute emboli from endocardial vegetations. Clinically it presents as a complication of bacterial endocarditis rather than a disease of the kidney, and it will not be discussed further in this chapter.

(3) *Chronic pyelo-nephritis.*—The acute suppurative lesions of the kidney will more fittingly be discussed in a later section, but it is proper to point out here that the late results of renal suppuration may be very similar to those of chronic glomerular nephritis; that in a certain number of cases of renal dwarfism and of renal failure with hypertension the "small white kidneys" found at autopsy are scarred and ischæmic organs in which the initial insult was caused by a suppurative pyelo-nephritis.

Nephrosis

The term nephrosis is used to denote those forms of Bright's disease characterized by primarily degenerative lesions of the renal parenchyma, with the main damage falling on the tubular epithelium; it includes several different conditions.

(1) *Larval nephrosis* is the term applied to slight renal lesions manifested solely by albuminuria, *e.g.* febrile albuminuria.

(2) *Necrotizing nephrosis*, characterized by the necrosis of tubular epithelium, with impairment of function, is seen typically in acute mercurial poisoning.

(3) *Lipoid nephrosis*, characterized by slow degenerative lesions in the renal epithelium, with persistent œdema and albuminuria but without

hypertension and without a tendency to failure of renal function, is a condition whose existence as a separate entity is still violently contested. By many pathologists it is looked upon as a variety of glomerular nephritis, in which the glomerular lesions are minimal in the earlier stages, while Ellis maintains that cases diagnosed as lipoid nephrosis form a continuous series with other cases which gradually progress to hypertension and renal failure; to this whole group he applies the term "Type II nephritis." It is true that differentiation between lipoid nephrosis and "nephrotic nephritis" may be extremely difficult; but we have been struck by patients who have made complete recoveries after lying waterlogged for months, and, at the other extreme, by those, dying early in the disease, in whom histological examination reveals no glomerular damage whatsoever. We feel, in the company of other pædiatricians, that we are fully justified in continuing to describe lipoid nephrosis as a separate entity—and of a series of 215 cases of Bright's disease treated in two Newcastle hospitals we have placed 18 in this category.

Whether lipoid nephrosis is primarily a disease of the kidney, or whether, as in Bence-Jones' proteosuria, the renal damage is secondary to the albuminuria, we cannot say. If the latter view be correct, the disorder is primarily one of protein metabolism, and some authors have stated that the albumin excreted in the urine in lipoid nephrosis differs from normal serum albumin.

The kidney is enlarged and the capsule strips readily, leaving a pale smooth surface—under older classifications these cases would have been named "large, pale kidney" and "chronic parenchymatous nephritis." The substance of the kidney is greasy and the cortex pale or yellowish in colour, standing out from the darker medulla. The typical histological lesions are degenerative changes in the tubules, which are dilated, without any of the proliferative changes of inflammation. There is a heavy deposit of lipoid in the tubular cells which show double refraction with the polarizing microscope. The glomerular changes are relatively insignificant; in long-standing cases there is thickening of the basement membrane, but in patients dying early in the disease the glomeruli may be entirely normal.

(4) *Amyloid nephrosis* is, at least in childhood, almost a disease of the past. Presenting with abuminuria and œdema, and resembling initially lipoid nephrosis, it tends to be progressive and to lead to failure of renal function and to hypertension.

(5) *Lower nephron nephrosis* is the term applied to the renal disorders associated with incompatible blood transfusions, blackwater fever, crush syndrome and certain cases of sulphonamide poisoning. It is seen also in hæmolytic disease of the newborn. The mechanism is not fully understood, but the work of Trueta and his colleagues suggests a neuro-vascular mechanism, with shunting of blood from the cortical glomeruli. The changes are seen chiefly in the distal tubules, *i.e.* in the ascending limbs of Henle's loops and in the distal convoluted tubules. The tubular cells show severe degenerative changes and contain eosinophilic granules. In places they may be desquamated, and direct tubulo-venous communica-

tions may occur. Characteristically the lumina of the tubules are filled with pigmented debris, a finding which led to the view, now discredited, that renal failure was due primarily to tubular blockage.

Nephrosclerosis

The renal lesions of essential hypertension—" small red kidney," " primary contracted kidney " or " chronic interstitial nephritis "—are to be seen generally in adult life, but Court has collected from the literature twelve cases of malignant hypertension, apparently primary, in childhood. In addition, it is probably true that secondary hypertension plays a considerable part in producing the late changes in kidneys already the seat of some other lesion, *e.g.* chronic glomerular nephritis or chronic pyelo-nephritis. Considered in this light, the changes of nephrosclerosis are not so uncommon. These changes are essentially those of ischaemic atrophy, with intimal thickening of the smaller arterioles, and degenerative changes in glomeruli, which ultimately become small knots of connective tissue. The associated tubules also atrophy, other nephrons become hypertrophied, and the kidney as a whole is irregular and scarred. When the hypertension is of the malignant type the renal changes more resemble those of acute nephritis, with swelling of glomeruli and formation of epithelial crescents ; the arteriolar changes are more evident, and amount to arteriolonecrosis.

Congenital hypoplastic kidneys

The term congenital hypoplastic kidneys is proposed for those examples of " small white kidney " seen in renal dwarfism where the histological appearances suggest the failure of development of nephrons rather than their destruction by inflammatory or degenerative processes.

Miscellaneous

(*a*) Ellis in his classification of Bright's Disease, describes an important group as type II nephritis, and includes in this nephrosis. He associates a clinical picture of insidious onset of œdema and albuminuria, rarely followed by recovery and almost always progressing slowly to hypertension and renal failure, with a pathological picture of tubular degeneration and glomerular changes consisting of bland necrosis and capsular adhesions progressing to proliferative glomerulitis with hyalinization. These conclusions are drawn from a large series of cases of Bright's disease in whom adults preponderate, and we have endeavoured to obtain a perspective in childhood. Of a series of 215 cases of Bright's disease in infancy and childhood 25 only would fall into the class of Ellis type II, and of these we consider 18 to be examples of lipoid nephrosis.

(*b*) A further type of renal disorder of childhood is that associated with the names of de Toni and Fanconi. The disorder is probably primarily metabolic, and the renal changes appear to be secondary. The clinical syndrome is one of hypophosphatæmic rickets and dwarfism associated with aminoaciduria, glycosuria, albuminuria and later renal

failure. The renal changes consist of progressive destruction of glomeruli and tubules with scarring.

(*c*) Nephrocalcinosis is the name applied to the pathological finding in the distal convoluted tubules and collecting tubules, and also in the surrounding connective tissue, of deposits of calcium. These deposits are on occasion sufficiently dense to be demonstrable radiographically. Lightwood drew attention to a connection between these autopsy findings and a clinico-biochemical syndrome of infancy characterized by failure to thrive and a hyperchloræmic acidosis. The syndrome is now referred to as " Lightwood's syndrome," " nephrocalcinosis infantum," " renal acidosis of infancy " and " idiopathic hyperchloræmic acidosis of infancy." There are, however, other causes of similar renal calcification, and MacGregor was able to find 44 examples of such calcification in autopsy material, in only 24 of which was there a clinical history of the Lightwood syndrome.

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CLINICAL TYPES AND MANAGEMENT OF BRIGHT'S DISEASE

Acute nephritis

It is fortunate for the pædiatrician and his patients that acute nephritis is by far the most common form of Bright's disease seen in childhood; for the pædiatrician as it is the form most easily recognized and under-

stood ; for the patient on account of its excellent prognosis. Out of a Newcastle series of 215 cases of Bright's disease in childhood 177 were of acute nephritis.

Acute glomerular nephritis affects the sexes equally ; for reasons not as yet understood it is extremely rare under the age of eighteen months and has its maximum incidence in later childhood. Many writers have stressed the importance of infections in its causation, in particular infections with the hæmolytic streptococcus. The majority of these infections are from streptococcal diseases of the nasopharynx, ear or upper respiratory passages, with acute tonsillitis, otitis media and scarlet fever as the best-known examples. From the combined results of Hill, Volhard and Fahr, Wyllie and Moncrieff, comprising 214 cases of acute nephritis, there were 66 instances of acute tonsillitis and 25 of scarlet fever immediately preceding the illness ; and only 37 instances in which there was no apparent infection to which the cause could be attributed. Otitis media, infected wounds, impetigo contagiosa, parotitis, cervical adenitis, erysipelas, pneumonia and empyema were other prominent causes. In our experience a whitlow is not an uncommon precursor of acute nephritis. The association of acute infectious fevers and nephritis can be judged from Rolleston's figures. In 150,000 cases of scarlet fever 3·58 per cent., in 57,000 cases of diphtheria 0·57 per cent., and in 747 cases of measles 0·13 per cent. developed acute nephritis. Streptococcal diseases—scarlet fever, tonsillitis—are so obviously the chief infections which precede this form of nephritis that when it is found to follow measles and other illnesses it is highly probable that it is due to accompanying streptococcal complications rather than to the initial illness.

Although recent clinical investigations have upheld the role of infection in the causation of acute nephritis, it is true that a history of exposure to cold preceding the attack can often be obtained, and the old view that cold and exposure play a causative role should not too readily be discarded. The changes of acute nephritis are primarily vascular in origin, and external cold has a profound influence on the vascular bed of the whole body.

Pathology.—Acute nephritis is a single entity, and the pathological changes have already been briefly described. It can be reiterated that the primary changes are in small vessels throughout the body, being the result of interaction between streptococcal antigen and antibody ; in the kidney the glomeruli are damaged by these vascular changes.

Symptoms and signs.—The clinical picture varies in severity from a symptomless appearance of a little blood in the urine a few days after a sore throat, to a serious or even fatal illness with hæmaturia, oliguria, œdema and uræmia.

In a case of moderate severity the child wakens one morning, about a fortnight after having had a sore throat, feeling "out of sorts," and his mother notices that his face is pale and puffy. His urine is dark in colour. If seen at this stage, the child is pale and has moderate œdema of face and extremities. His blood pressure is a little raised—say to 130/90—but physical examination otherwise reveals nothing abnormal. His urine output is diminished, and the urine is dark brown and opaque.

The boiling test shows a heavy cloud of albumin, and on microscopy there are numerous red blood cells, and some leucocytes and cellular and granular casts. For a day or two the œdema remains or increases, and the urine remains small in quantity and bloody, but within a week the œdema is diminishing, and the urine is increasing in quantity and becoming paler. Within three weeks the child feels well and has lost his œdema ; the urine looks normal to the naked eye, but still contains a trace of albumin and, microscopically, a few red blood cells and granular casts. The blood pressure has returned to its normal level of, say, 105/65. At the end of six weeks the child is fully recovered, though a trace of albumin may remain in the urine for several months, often disappearing when the child is recumbent, to return when he resumes the erect posture.

In order to depict the many variations on this basic pattern it is probably best to consider individual symptoms and signs.

The general symptoms, usually consisting simply of malaise, may be completely absent, or, on the other hand, may be much more severe and include fever, headache, backache, nausea and vomiting. It is seldom that these persist for more than a week in a child who is to make a complete recovery.

Visible œdema may be absent in mild cases ; commonly it is evident as puffiness of the eyes and pitting on pressure above the ankles ; only rarely is there gross generalized œdema with ascites. Œdema has usually disappeared within a fortnight, and its persistence after this portends an unfavourable outcome.

The urine is nearly always diminished in quantity in the early stages, and total anuria may occur at the onset or supervene after a few days ; rarely does it persist for more than forty-eight hours. The urine output has usually returned to normal within a week, and there may be a diuresis as the œdema subsides. Albumin is present in amount varying from a faint trace to a very heavy cloud ; its amount is usually greatly reduced within three weeks, and after six weeks only a faint trace should be present if full recovery is to occur. Blood is present at the onset in varying amounts ; the urine may appear almost like pure blood, commonly it is brown and " smoky," while at times only a few red cells may be present on microscopic examination. Obvious blood on naked eye examination usually clears in a week, and after six weeks there should be only an occasional red blood cell on microscopic examination. White blood cells and casts should disappear in about the same time. The time of apparent return to normal of the urine will vary with the zeal with which it is examined ; though routine examinations commonly reveal nothing abnormal apart from a faint trace of albumin after six weeks. Addis counts still show an increased excretion of red cells, leucocytes and casts, which may persist for several months.

The blood pressure is commonly moderately raised at the onset, and occasionally such levels as 200/160 may be reached at the onset or a few days later. In the majority of cases return to normal occurs within three weeks. In association with this hypertension, and, especially with sudden rises in blood pressure, hypertensive cerebral attacks, with con-

vulsions, coma or transient blindness may occur. They seldom last for more than forty-eight hours, and in themselves they are not of serious prognostic import. Though always associated with hypertension, their occurrence can not be correlated with the absolute height of the blood pressure.

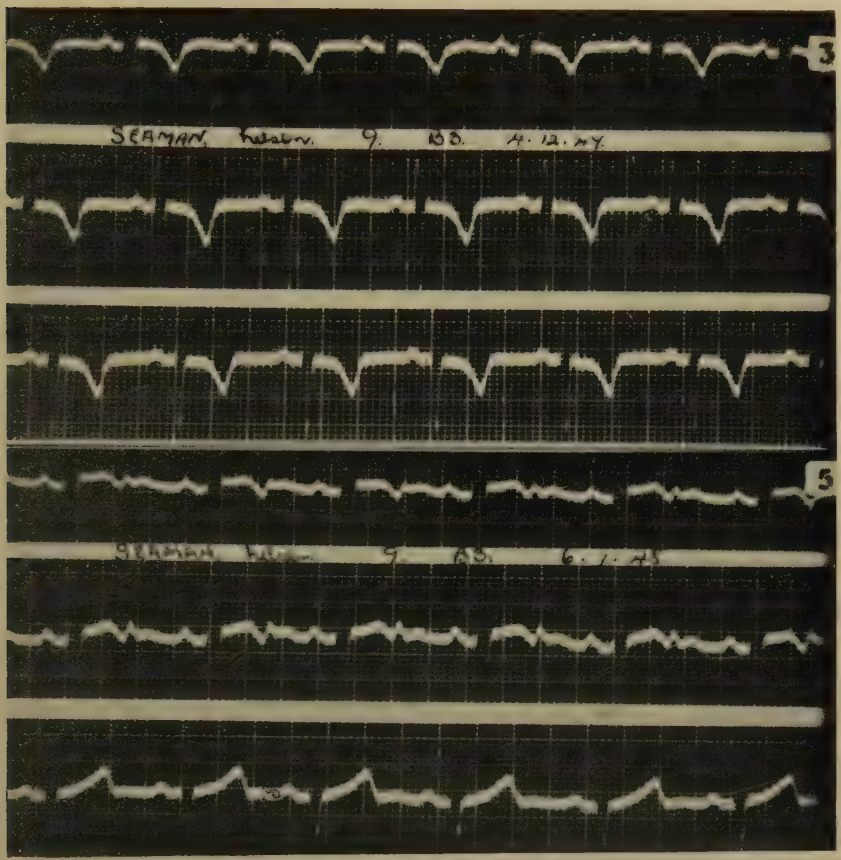

FIG. 539.—ELECTROCARDIOGRAMS OF A BOY OF NINE YEARS SUFFERING FROM ACUTE NEPHRITIS WITH GROSS CONGESTIVE HEART FAILURE.

The upper three tracings are of præcordial leads taken on admission to hospital and show evidence of myocardial damage. The lower three tracings are of the same leads one month later showing return to normal.

Goodhart in 1879 recognized the involvement of the heart which can occur in acute nephritis, and spoke of "acute dilatation of the heart as a cause of death in scarlatinal dropsy." It is only within recent years, however, that the frequency of such involvement has become clear, and it is probable that in a third or quarter of all cases of acute nephritis there is some myocardial damage. In only about 5 or 10 per cent. of cases, however, is this damage such as to produce manifest heart failure, and,

except when it leads to a fatal termination—heart failure being one of the few causes of death in acute nephritis—complete recovery of the heart muscle is the rule. The myocardial changes are almost certainly the result of injury to the small vessels, which occurs in the original systemic antigen-antibody reaction; though hypertension is usually present in cases with myocardial involvement, and though this may increase the burden on the heart and precipitate failure, it is unlikely that the cardiac damage can be attributable to hypertension *per se*. The clinical evidences of heart involvement vary considerably. Sometimes it can be detected only by electrocardiography (fig. 539) or by the demonstration radiologically of cardiac enlargement (fig. 540 and 541). In other cases the cardiac impulse may be displaced to the left, and there may be muffling of the first sound with a soft systolic murmur at the apex. Finally, there are those cases in which there is gross cardiac failure; this sometimes involves chiefly the left ventricle, producing pulmonary œdema with cough and intense dysnoea and distress, while at other times failure of the right heart leads to fullness of the neck veins and swollen, tender liver.

It should be made clear that there is no correlation between the severity of the different clinical manifestations of acute nephritis. For example, one child admitted to hospital with severe heart failure may have minimal urinary changes, while another with gross hæmaturia may have little systemic upset.

Careful renal function tests will usually reveal some degree of renal impairment in the early stages of nephritis, but it is seldom that such tests are called for at this stage, and it is common for the blood urea to be only a little raised; figures of over 100 mgm. per 100 c.cm. are uncommon. Another laboratory test frequently employed is determination of the erythrocyte sedimentation rate. This is almost invariably high in the early stages, readings of over 100 mm. in one hour (Westergren) being common. A fairly rapid fall occurs in the first two or three weeks after which the rate of return to normal becomes very slow, and Brod has shown that a moderately raised sedimentation rate may remain for several months. The hæmoglobin is usually a little lowered, and occasionally severe anæmia may occur.

Course and prognosis.—Acute nephritis in childhood carries a good prognosis, about 75 per cent. of cases ending in complete recovery. The application of the Addis technique led some observers to the view that a large proportion of cases entered a latent phase, destined later to show the manifestations of chronic nephritis, but it now seems likely that they did not appreciate that microscopic hæmaturia might persist for several months in cases going on to complete recovery, and Ellis, Snoke and Giles have published series showing a full recovery rate of 75 per cent. Of the remaining cases a small number, about 4 or 5 per cent. of the total, die early in the illness, death being due to heart failure, uræmia or infection. In a similar proportion the early symptoms fail to clear up, hæmaturia persists, the œdema increases, and the child enters the subacute or nephrotic phase, which almost invariably ends with death after an

FIG. 540.—RADIOGRAPH OF A BOY OF SEVEN YEARS WITH ACUTE NEPHRITIS WITH GROSS CONGESTIVE HEART FAILURE, DEMONSTRATING MARKED CARDIAC ENLARGEMENT.

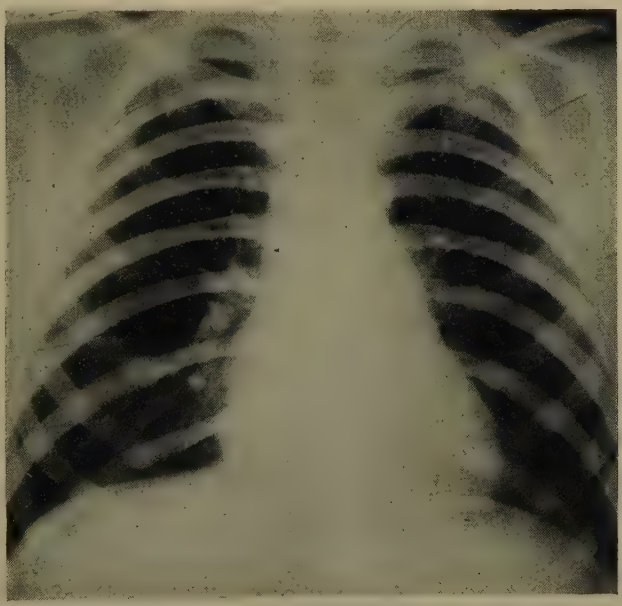

FIG. 541.—RADIOGRAPH OF THE SAME PATIENT AFTER RECOVERY, SHOWING RETURN OF HEART SIZE TO NORMAL.

interval of weeks or months. In the remaining 15 per cent. recovery at first appears to be taking place, but some small evidences of activity remain a slightly raised blood pressure, recurrent slight œdema, or persistence of red blood cells and casts in the urine in numbers too great to be ignored. In these cases the disease enters a latent phase, which may last for many months or years, but ultimately symptoms and signs of hypertension and renal failure develop, and the patient dies of chronic nephritis.

Such is the prognosis of acute nephritis in general, but the practitioner's task is to attempt to assess the prognosis in an individual case. In so doing, his first golden rule must be this—that the severity of the symptoms of onset has no bearing on the ultimate prognosis ; therefore, the frequency of recovery being so much greater than that of death or chronic illness, he is fully justified in taking an optimistic view of every case of acute nephritis seen at onset, however ill the child may be. We have seen a child who made a complete recovery after being anuric for eight days, and several who have been restored to health after suffering from eclamptic convulsions or severe heart failure. It is not on the severity of the symptoms but on their duration that prognosis rests ; the persistence of œdema, macroscopic hæmaturia or hypertension for over three weeks should make prognosis guarded, and if any of these symptoms persists for over six weeks an unfavourable outcome is almost certain. The Addis technique is of value in detecting latent chronic nephritis, but it must be reiterated that abnormal values may persist for several months without of necessity indicating chronicity. Erythrocyte sedimentation estimations are of little value in prognosis.

Diagnosis.—The diagnosis of acute nephritis is usually rendered easy by the characteristic clinical picture, but occasionally difficulty may be met in differentiating between it and other diseases of the urinary tract ; such difficulty may occur when an acute pyelo-nephritis is accompanied by gross bleeding. It is a safe rule that symptomless hæmaturia should be considered as due to acute nephritis until proved otherwise. An acute exacerbation of a chronic nephritis may prove very deceptive, but Kellett's work suggests that estimations of blood complement may be of great help in this connection ; a low or absent complement is almost diagnostic of acute nephritis, while in an exacerbation of chronic nephritis the complement remains normal. When presenting symptoms at onset as those of hypertensive cerebral attacks or acute heart failure, the true diagnosis may at first be obscured. It should be borne in mind that hypertension in childhood is commonly due to acute nephritis. Again, the sudden onset of acute heart failure in a child previously apparently healthy is a rare event ; when it does occur, acute nephritis is the likely cause. We have maintained this diagnosis in a child with congestive heart failure and hypertension, despite a normal urine on his admission to hospital.

Treatment.—Treatment in the early stages of acute nephritis is simple, consisting of rest, warmth and dietary restriction. The first decision to be reached is as to whether the child should be nursed at home

or in hospital; the answer will depend to some extent on the severity of the illness, but even more on home circumstances. When the parents are reasonably intelligent and co-operative, and when the child can have his own bed in a warm room, any case of acute nephritis of moderate severity, but uncomplicated, can well be nursed at home. But when the home is damp or overcrowded, or when complications, such as hypertensive fits or heart failure, supervene, it is best for the child to be removed to hospital. Whether he be at home or in hospital, and however mild the illness may appear, the child should at the onset be kept at complete rest in a warm bed; it is quite unnecessary to subject him to the discomfort of lying between blankets. Again, however mild the symptoms, food should be entirely withheld in the first few days, and fluid should be restricted to 30 ounces per day for a child of five or six years, and should consist of water, glucose water, orange juice or barley water. In hospital it is a kindness to the child to nurse him in a single room at this stage, so that he is not subjected to the ordeal of watching other children eat while he must go hungry. We believe that stringent rest and starvation in the first few days are of the utmost importance. Drugs, on the other hand, play little part. Diuretics must be completely avoided. Penicillin should be administered whenever there is reason to believe that the causal streptococcal infection remains active. The anti-histaminic drugs have been recommended, but valid evidence of their value remains lacking.

The great difficulty in the treatment of acute nephritis lies in the determination of the duration of the various stages. It is important that a careful record of progress be kept, including daily notes of œdema and blood pressure; daily weighing, when feasible, is a valuable guide to the extent of œdema. All urine passed should be kept, and the twenty-four hour collection measured each morning, inspected for blood by naked eye and tested for albumin. As the naked eye blood disappears, microscopic examination should be made at intervals. The patient should remain at complete rest in bed until œdema has gone, the urine is clear to the naked eye, and the blood pressure has returned to normal. He should remain in bed, but with some increase in activity, until all but a trace of albumin has cleared from the urine, and microscopic examination reveals only an occasional red blood cell. In all but the mildest cases bed-rest for from four to six weeks will be the rule. If at the end of three months hæmaturia, œdema or hypertension should remain, complete recovery is so unlikely that further treatment should be directed to preserving the child's happiness rather than his life, and bed-rest should no longer be enforced. In the child who is progressing well, the period of bed-rest should be followed by about a fortnight indoors, and he should be allowed out of doors for about a further fortnight before returning to school.

After the first two or three days the fluid intake should be regulated according to the urine output; as this increases so can the intake be increased, and when the output is normal unlimited fluids can be given. If possible nothing but the bland fluids mentioned should be given until gross naked-eye blood has disappeared from the urine. Humanity may

force this rule to be broken if the gross hæmaturia persists for more than a week. Once the urine is clearing milk, bread and butter, and biscuits can be added to the diet, and rapid increase should be made so that ordinary light diet is being consumed within a week of the first additions. After another week normal food can be taken. It is our belief that starvation should be strict but not prolonged, and that, once the early symptoms have cleared, there is no point in protracted low-protein diet.

A daily bowel action is desirable during the illness, and it may be necessary to give mild aperients to achieve this, but strong purges are to be avoided. Any simple aperient, such as syrup of figs, magnesia or salines, may be used, preferably one which the parents have been accustomed to give to the child.

During convalescence anæmia—as distinct from vascular pallor—may call for the administration of iron.

Complications call for their own special treatment, and the management of anuria, uræmia and hypertensive cerebral attacks has already been discussed. When heart failure occurs the child should be propped up in bed in the most comfortable position; atropine should be given for acute pulmonary œdema, and opium may be needed if there is extreme distress or restlessness —15 minims of tincture of opium or $\frac{1}{12}$ grain of morphine being administered to a six-year-old child, and repeated as needed. Digitalis also is indicated, though its dosage is difficult to regulate. At the outset one grain of powdered digitalis leaf or $\frac{1}{240}$ grain of digitalin Nativelle may be given six-hourly to a child of six years, and the general condition of the child, rather than the pulse rate, will be the guide to further administration.

Finally, some reference must be made to the problem of tonsillectomy in relation to nephritis. Widely divergent opinions are held on this, but we consider that the decision should be reached on the history, without regard to the nephritis or to the size of the tonsils. We hold that the operation is indicated when there is a history of several attacks of tonsillitis; it should, if possible, be postponed until the child has recovered from his nephritis, and should be "covered" by the administration of penicillin for four days.

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Chronic Bright's disease with œdema
(including Lipoid Nephrosis)

The clinical syndrome of chronic Bright's disease with œdema differs in important respects from acute nephritis, just described; it is not nearly so common—25 cases as against 177 in a Newcastle series—the prognosis not nearly so favourable, and it is not a pathological entity constituted of a single disease process. It includes cases which are a sequel to acute nephritis, cases of lipoid nephrosis, and other cases which are difficult to classify.

Pathology.—It is difficult to forecast in any given case what changes will be found at autopsy, though the kidneys will usually be swollen and pale. Histological examination will sometimes reveal the changes already described as those of subacute glomerular nephritis, and sometimes those of lipoid nephrosis.

Ætiology.—In those patients in whom the symptoms have followed acute nephritis, the ætiological factors already described for this condition will have been operative, though it is not known why some cases of acute nephritis should progress to this chronic œdematous phase when so many more recover completely and quickly.

In contrast to acute nephritis, and contrary to opinions often expressed, lipoid nephrosis is largely a disease of infancy and early childhood. Heymann and Startzman found that of thirty-four cases in children 64 per cent. were under the age of three years at onset, while in twenty-two cases collected by Clausen ten occurred between the ages of one and five, and eight between the ages of three and seven years. In most cases no cause can be found, but occasionally the disease follows diphtheria, pneumococcal infections, syphilis, and poisoning with organic substances. Little support can be found for the views that it always follows pneumococcal or staphylococcal infections. The possibility that it is initially a general disease of metabolism with secondary renal changes has already been discussed, and it is true that in certain instances the œdema may precede the albuminuria.

Symptoms and signs.—All forms of chronic œdematous Bright's disease have in common an insidious onset, gross œdema, often involving the serous cavities, and gross albuminuria.

In a typical case of nephrosis the first symptom noted is œdema, and the first site is commonly the scrotum. The œdema gradually increases and becomes generalized, involving the face and limbs, and the abdomen becomes swollen, with ascites and œdema of the abdominal wall (fig. 542). Sometimes, particularly in young infants, the onset of œdema may be sudden and generalized; in other cases, frequent shifting of the œdema may be noted, so that regular weighing rather than mere observation should be the guide to the degree of water retention. Sometimes the œdema may appear strangely in unusual sites; it may first be seen in one limb, and in one of our cases a sudden œdema appeared between the clavicle and the jaw to be followed the next day by the generalized œdema of nephrosis.

In the early stages of the illness the child does not feel ill, though he may be greatly inconvenienced by the œdema, and on physical examination no abnormalities are noted apart from the pallor and œdema. In particular the blood pressure and eye grounds are normal.

The urine is reduced in amount and commonly contains large quantities of albumin; occasionally at the onset of the œdema albumin may be absent from the urine, but it is rarely that the patient is seen at this early stage. Microscopic examination of the urine reveals the presence of a few leucocytes and granular or fatty casts; the presence of red blood cells will always cast doubt on the diagnosis, though occasionally a few may appear after an infective episode. Chemical examination of the blood regularly shows a hypoproteinæmia, the albumin level being especially affected, so that there is a reversal of the normal albumin—globulin ratio; at times the total serum proteins may fall below 3 per cent., with a serum albumin of below 1 per cent. A related finding is that the plasma amino acid nitrogen is constantly low, seldom being above 3 mgm. per 100 c.cm., and a further constant finding is a lipæmia with high blood cholesterol readings. In contrast, the blood urea is seldom above normal. Urea clearance tests show a normal or enhanced renal function.

FIG. 542.—CASE OF NEPHROSIS.

Œdema for 4 months. Marked albuminuria. Only occasional red blood-cells in the urine. Blood urea, 15–28 mgm. per 100 c.cm. Renal function tests normal. Blood cholesterol, 430 to 590 mgm. per 100 c.cm.

The course varies greatly. In a few cases, especially in young infants, complete recovery occurs after a few weeks. More often the illness runs a fluctuating course of many months, while occasionally a period of several years, marked by periods of remission and relapse, may pass before the illness terminates in recovery or death. Sometimes an intercurrent infection, especially measles, is followed by diuresis and recovery, but it is more common for septic complications, especially pneumococcal septicæmia and peritonitis to which these children are peculiarly liable, to lead to a fatal termination. The prognosis is probably better than is generally believed, and recovery rates of 30 and 40 per cent. have been reported.

A peculiar feature of chronic nephrosis is the occurrence of "nephrotic crises," in which, to the accompaniment of fever, the child becomes critically ill and extremely œdematous. In some of these crises pneumococcal septicæmia or peritonitis is present, but in other cases, in which the clinical picture is identical, no infection can be demonstrated. As

the pneumococci are often identical with organisms found in the throat, and of types of low pathogenicity, it is possible that their presence is an effect rather than a cause of the crisis, which may rather be biochemical in origin, as a constant finding is a fall in the blood amino acid nitrogen to below 2·5 mgm. per 100 c.cm.

Whereas most of the infective complications of nephrosis are well recognized, one which has received little attention is a curious infection of the œdematous subcutaneous tissue, akin to erysipelas but without the striking visible changes of this condition. The child becomes irritable, febrile and ill, and complains of pain in the trunk, limbs or face. On examination of the site of the pain the subcutaneous tissue is found to be indurated and exquisitely tender; initially there is no colour change, though redness may ensue. When the pain is abdominal confusion with peritonitis may readily occur, but experience enables one to differentiate the tender induration of the abdominal wall from the tenderness and rigidity caused by an underlying peritonitis. Rapid relief of the symptoms usually follows the exhibition of penicillin.

When, in the course of nephrosis, spontaneous copious diuresis occurs, one is struck by the severe wasting of the child, previously masked by the gross œdema.

In that form of chronic Bright's disease following acute nephritis, there are many features in common with nephrosis, notably the gross œdema and albuminuria, low serum proteins and high blood cholesterol. The onset, however, is different, as the illness is consecutive to acute nephritis; there is therefore usually puffiness of the eyes and hæmaturia preceding the gross generalized œdema. Though routine microscopic examination of the urine on isolated occasions may reveal no red blood cells, their presence will be detected by repeated examinations, while an Addis count will show that they are being excreted in abnormal numbers. The blood pressure, also, is almost invariably raised, though the rise may be only slight for several weeks or months. Again, the blood urea is usually raised, and urea clearance tests will reveal impairment of renal function. The course of this chronic glomerular nephritis is one of irrevocable progress to death; sometimes this occurs from intercurrent infection after the patient has lain waterlogged for months, while in other cases the œdema gradually clears, only to be replaced by evidence of renal failure leading to death from hypertension or uræmia.

There are, finally, those cases of œdematous Bright's disease, fortunately uncommon in childhood, in which there is no history of acute nephritis and in which the onset is that of nephrosis, but in which microscopic hæmaturia, hypertension and evidence of impaired renal function point to glomerular damage. These are the cases which Ellis includes, together with nephrosis, in his type II nephritis. It may be that some of these cases are in reality examples of chronic glomerular nephritis in which the acute attack has been so mild as to be insignificant; or they may be cases of nephrosis in which the glomeruli have been damaged by the persistent albuminuria. If the latter be true, then the chief difference between the views of Ellis and of the authors is one of terminology. From the stand-

point of the practitioner, however, it is convenient to divide the cases of chronic œdematous Bright's disease into nephrosis, with its reasonable hope of recovery, and chronic glomerular nephritis with its uniform fatality, and to group the borderline cases with the latter.

Diagnosis is concerned chiefly with differentiation between the different forms of chronic Bright's disease with œdema. Rarely does a severe case of generalized angioneurotic œdema, which may be accompanied by albuminuria, give rise to difficulty, and progress soon makes the diagnosis clear. The diagnosis of nephrosis rests on the absence of hypertension, absence of blood from the urine, though a few red cells may be seen microscopically following an intercurrent infection, and the normal renal function. The diagnosis of chronic glomerular nephritis will usually be made when there is a history of a preceding acute attack. When there is no such history of an acute nephritis, but the presence of blood in the urine, the height of the blood pressure or evidence of nitrogen retention argue against nephrosis, it is, in the present state of knowledge, probably better to acknowledge defeat in diagnosis, though this by no means implies inability in either prognosis or management.

Prognosis rests in the first place in differentiating true nephrosis from the other forms. If all the evidence points to true nephrosis there is a 30 to 40 per cent. chance of full recovery ; the younger the child the better the prospect, but, otherwise, there is at present no means of saying which child will die or which will recover, and it is in any case likely that the illness will be long and tedious. If, however, there are unmistakable signs of glomerular damage or impairment of renal function, so that the case can no longer be looked on as one of nephrosis, a fatal outcome would seem inevitable after a period usually measured in months.

Treatment.—No means of influencing the renal changes in any of the diseases under consideration are known ; treatment is directed therefore at sustaining nutrition, combating infections and relieving symptoms.

As the illness is likely to be long it is best for the child to be nursed at home for most of the time, if this is at all feasible ; admission to hospital is advisable for short periods only, for assessment and for treatment of complications. The severity of the œdema will compel rest in bed for long periods, but there is no reason for the child to be prevented from getting up whenever he is anxious and able to do so.

As the level of the plasma proteins is low, and as protein is constantly being lost in the urine, a high protein diet is indicated. One containing about 1·5 grammes of protein per lb. of ideal body weight, that is the body weight to be expected in the absence of either wasting or œdema, is best, and Farr has shown that there is nothing to be gained by higher protein intake, or by abnormally high carbohydrate intake. A low sodium intake is theoretically desirable, but the resulting diet is apt to be unpalatable, and it is unwise to risk the child's nutrition or morale by attempting to enforce it.

Attempts have been made to reduce the absorption of sodium without drastically lowering the sodium in the diet by the use of " cation exchange resins." These substances, which have been used widely in commerce,

are compounds which will accept certain ions from solutions, releasing equivalent quantities of other ions in exchange. Thus a suitable resin consisting of a mixture of potassium and ammonium compounds will, when placed in a solution containing sodium ions, take up a number of these ions and liberate into the solution an equivalent number of potassium and ammonium ions. If one of these resins is administered therapeutically it will remove sodium ions from the intestinal contents, and will produce an effect similar to a low sodium diet. A difficulty is that other ions, such as calcium, may be accepted by the resin, and a considerable disturbance in the ionic balance of the body fluids may result unless dietary precautions are taken, controlled by biochemical examinations. This treatment is, therefore, suitable for use only in hospitals with adequate biochemical facilities. At best it is but a palliative, and it remains to be shown that the advantages of this form of treatment in nephrosis outweigh the disadvantages. For further details the reader is referred to the papers of Payne and Wilkinson (1951) and of McChesney, Dock and Tainter (1951).

When infections supervene, prompt treatment by the appropriate antibiotics is essential.

The chief symptom calling for treatment is the œdema. As this is due primarily to the low plasma protein content attempts to raise this content are logical, but not of great practical value. Intravenous infusion of double strength reconstituted plasma or serum, about two pints being given by slow drip to a child of five or six years, may lead to temporary improvement in the œdema, and is worth trying at periods when the morale of child or parents has sunk to a low ebb. Intravenous acacia has been used, but has no advantages over plasma. Diuretics can also be used in similar circumstances, but not routinely for long periods. Urea is best for the purpose. When all other measures have failed, it is permissible to try mersalyl in an older child, but there is always the risk of sudden, and may be fatal, collapse, and it should not be given to an infant.

From time to time Southey's tubes may be used with advantage to drain ascites or gross limb œdema.

Thyroid has been recommended, but there is no real evidence of its value. As dramatic recovery has in a few instances followed an infective illness, especially measles, one is tempted to try this as a therapeutic measure; but only under special circumstances would it be justifiable to expose a nephrotic child to measles, and withholding of chemotherapy in other infections is never justifiable.

Mention must be made of the use of ACTH. When this is given in a dosage of 12·5 mgm. intramuscularly every six hours for eight to twelve days a copious diuresis usually results with considerable relief to the patient. The diuresis may occur during the period of administration, but more commonly it takes place a few days after the hormone has been discontinued; it may or may not be accompanied by disappearance of albumin from the urine. The action of ACTH can be compared with that of an attack of measles; sometimes there results diuresis and an apparently

complete cure of the illness, more often œdema reaccumulates after a variable period of well-being, while occasionally the hormone has no apparent effect on the course of the illness. The use of this hormone is still in the experimental stage and it is not yet possible to state dogmatically whether or not ACTH should be used in any given case of nephrosis, nor at what stage in the illness it should be given. Its use, moreover, is not without risk of biochemical and infective complications, and at present it should only be administered in hospital. Further information is contained in the writings of Barnett *et al.* (1950, 1952).

The treatment of nephrotic crises calls for special comment. As many of these are associated with pneumococcal infections treatment with penicillin is logical, but Farr maintains that the best results are obtained by the administration of protein hydrolysate intravenously; he recommends a dosage of 50 to 70 grammes per day to a child of five to seven years. Great care must be taken to avoid infection of the fluid being given.

The measures described are those applied to a nephrotic child in the hope of his recovery; the same treatment can be given to a child with chronic glomerular nephritis to relieve his symptoms, but without hope of cure. In such a case, however, the child's comfort and happiness are the first concern, and other considerations should be subordinated to them.

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Chronic Bright's disease with uræmia and hypertension

Although the forms of Bright's disease associated with uræmia and hypertension are closely related to those associated with dwarfism and rickets—indeed some cases could be placed equally well in either category—it is convenient to separate the groups for descriptive purposes. Both are, fortunately, rare diseases of childhood, and together they accounted for only 8 of 215 cases of Bright's disease in a Newcastle series.

Ætiology and pathology.—The clinical picture of chronic Bright's disease with uræmia and hypertension occurs whenever there has been such destruction and scarring of the kidneys that, on the one hand, the amount of functioning renal tissue left is insufficient to cope with the

normal metabolic needs of the body, while, on the other hand, the partial occlusion of blood vessels by the disease processes leads to hypertension by the mechanism of renal anoxia.

The sexes are affected equally, and the illness is seen more commonly in the later part of childhood. Sometimes the illness is clearly the sequel of an attack of acute glomerular nephritis, either as part of a continuous illness in which the phase of gross œdema already described passes gradually into the uræmic phase, or else being separated from the acute attack by a long latent phase, measured in months or years, of apparently good health. In other cases a prolonged attack of pyelo-nephritis in infancy is causally related to chronic uræmic nephritis of later childhood. Sometimes no history of antecedent illness can be obtained, and amongst these cases are those rare examples, referred to by Court, of malignant hypertension in childhood.

At autopsy, the naked eye picture is usually that of small, pale, scarred kidneys, and histological examination confirms the gross destruction of renal tissue with scarring, loss of architecture and obliterative vascular changes; the skilled histologist will determine whether these changes are those of chronic glomerular nephritis, of healed pyelo-nephritis or of malignant hypertension.

Symptoms and signs.—The onset of the illness, except where it is the immediate sequel of acute glomerular nephritis, is insidious, and weeks or months may elapse before medical attention is sought. There is, indeed, nothing specific about the early symptoms, the child merely becoming easily tired and disinclined to work or play. As the illness progresses symptoms characteristic of uræmia appear—headaches, anorexia, thirst, polyuria, vomiting, constipation or diarrhœa, and wasting. When first seen the child usually looks ill, being wasted, with sallow, dry skin and furred tongue. The blood pressure is usually raised, often considerably so, and the cardiac impulse may be forceful and displaced to the left. Occasionally the optic fundi show the changes of renal retinitis, but only in those cases in which hypertension is a prominent feature. The urine is increased in quantity, and is pale and dilute, the specific gravity being commonly in the region of 1010; it contains a trace of albumin, and microscopic examination reveals at the most an occasional red blood cell and hyaline cast. Blood examination often reveals a moderate normocytic anæmia, and a gross nitrogen retention, blood urea figures of 200 mgm. per 100 c.cm. being commonly seen. Renal function tests show marked impairment of the excretory capacity of the kidneys.

Changes in the levels of blood calcium and phosphorus may occur, but when these are marked the case is likely to fall into the category of renal rickets, to be described in the next section.

The picture may be complicated by the advent of hypertensive cerebral attacks, and on occasion these may be the symptoms which first bring the child under medical care. We have recently seen a boy of five years, who was admitted to hospital with convulsions followed by a transient hemiplegia. He had been in hospital for several months in infancy with

a chronic urinary infection, but had appeared to recover from this and to remain in good health until the onset of the cerebral symptoms. His blood pressure was 240/160, there was clinical evidence of marked cardiac enlargement, and there were numerous retinal hæmorrhages; his urine was copious, dilute and containing a trace of albumin. The convulsions did not recur, but he continued to suffer from headaches and vomiting.

Course and prognosis.—The illness ends inevitably in death, but the duration is extremely variable. In the case in which acute nephritis passes steadily into the chronic form, the total duration is likely to be measured in months, while an insidious onset may presage several years of moderate ill health before the fatal termination. Death occurs from uræmia, heart failure or intercurrent infection. In this form of nephritis hypertensive cerebral attacks are signs of ill omen, while evidence of progressive renal failure, such as a steadily rising blood urea, also points to an early termination.

Diagnosis.—In the early stages, when symptoms are vague, the diagnosis may readily be overlooked, but when a history of polyuria and thirst is added to that of general ill health, and when the findings include hypertension and a dilute urine containing a trace of albumin there should be little difficulty in recognizing that the patient is suffering from this form of Bright's disease. Difficulty may occasionally arise in distinguishing an exacerbation in chronic nephritis from acute nephritis, but the subsequent course should make clear the distinction. Diabetes insipidus must be differentiated, and in cases of doubt application of the urea clearance test will show impairment of renal function in chronic nephritis and none in diabetes insipidus. When the patient presents first with a hypertensive cerebral attack, primary intracranial disease will enter the differential diagnosis; the hypertension should, however, direct suspicion to the kidneys.

Treatment is directed solely towards maintaining the comfort and morale of the patient for as long as possible. Admission to hospital should be avoided except for short periods of treatment of complications, and in the terminal stages. The child should be encouraged to undertake normal activities including attendance at school so far as is possible. Although dietary restriction of protein reduces the load on the kidneys it also leads, over a long period, to malnutrition, and in general it is wise not to restrict the diet below that dictated by the child's appetite. Headaches can be treated with aspirin, codein compound or, in more severe cases, with pethidine.

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Chronic Bright's disease with dwarfism and rickets

The terms renal dwarfism, renal infantilism or renal rickets are used to describe a condition of stunted growth with rachitic bone deformities due to various forms of chronic kidney disease. For the recognition of this entity we owe much to the observations of Fletcher, Barber, Parsons and other English physicians. The clinical picture is seen in those cases of chronic renal disease in which prolonged impairment of renal function leads to disturbance of the normal calcium-phosphorus ratio of the blood. The type of renal disease leading to such disturbances of blood chemistry is similar to that causing uræmia as described in the last section; indeed it is difficult to know why chronic pyelo-nephritis, for example, should lead in one child to the type of illness just described, and in another to the clinical picture of renal rickets. It may be that the answer lies in the time of onset and degree of arterial hypertension. If hypertension is an early result of the renal disease it is unlikely that life will be prolonged after the onset of failure of renal function, and the patient will die with symptoms of uræmia and hypertension, as described in the last section. If, however, blood pressure is not significantly altered the patient may live for several years with impaired renal function, giving ample time for the manifestation of disordered bone growth. Renal dwarfism is a rare disease, but is a little more common than chronic Bright's disease presenting with hypertension and uræmia.

Ætiology and pathology.—Renal dwarfism or renal rickets may affect children of any age. It may be seen in young infants in whom the primary kidney disease is obviously congenital in origin. It may be observed first at the age of three or four years when the child's failure to grow or slowness in walking attracts attention, but in these again the history usually suggests a condition of impaired renal function dating from birth. In acquired kidney disease the bone symptoms appear at a later age in the form of adolescent genu valgum or "late rickets."

The primary kidney disease may be of various types so long as it is (*a*) severe enough to disturb the normal calcium-phosphorus ratio of the blood; and (*b*) allows the child to survive a sufficient length of time for the bone disease to develop and become apparent. The term "chronic interstitial nephritis" has often been applied to the kidneys found at autopsy, but this term now conveys only the meaning that the organs are small and scarred, and gives no indication as to the cause of these changes. It is only in a minority of cases that the clinical history and histological changes point to the illness being a true chronic glomerular nephritis. More often the kidney lesion is that of chronic pyelo-nephritis. We believe that in some cases there is a true congenital hypoplasia of the kidneys, though, even in these cases, there may be superadded inflammatory changes. At times there is hydronephrosis, with evidence of urinary obstruction, as, for example, a urethral valve. At other times, hydronephrosis is present without obvious anatomical obstruction, and Ellis and Evans, from a study of twenty cases, put forward the view that this is the most common finding. That type of renal rickets associated

with disturbances of amino-acid storage and excretion will be considered separately below. It will be clear that the nature of the disturbance of renal function, rather than the anatomical nature of the renal disease, is the important factor in the causation of renal rickets.

A little comment is needed on the chemical mechanism of the production of the bone lesions. The primary factor appears to be phosphate retention by the kidneys, and the most obvious explanation of the rickets is that it is a direct result of the disturbed calcium-phosphorus ratio, as in dietetic rickets. In many of these cases, however, hyperplasia of the parathyroids is found at autopsy, and Albright and others suggest that this is a response to the raised blood phosphate, and that the bone changes are in large measure a secondary result of the hyperparathyroidism. At autopsy, there is usually marked osteoporosis of the bone shafts in addition to the rachitic changes at the epiphyses.

FIG. 543.—BOY AGED SIXTEEN YEARS SHOWING THE SEVERE NATURE OF THE DEFORMITIES WHICH SOON OCCUR IN RENAL RICKETS.

Symptoms and signs.—In infancy the presenting symptoms are often polyuria and thirst, and the mother may remark that the urine is pale and "looks like tap-water." Failure to grow, or lateness in walking, may cause the child to be brought for advice, while, in the older child it is the occurrence of rachitic deformities which alarms the parents (fig. 543).

In all but early cases the general condition of the patient is that which may be expected from a state of chronic azotæmia. He is emaciated, with coarse, dirty, pigmented skin. Like Gilbert's precocious child who died "an enfeebled old dotard at five" he may appear shrewd and intelligent beyond his years. In stature the child may be less than half his lawful height. The bone deformities and weakness cause him to affect a waddling gait, and he stands usually in a position of genu valgum (fig. 544). Physical examination usually reveals no abnormality in the internal organs, but occasionally there may be hypertension and retinal changes.

The urine is characteristically copious and dilute, and contains a trace of albumin but no abnormal deposit on direct microscopy. Chemical examination of the blood reveals evidence of renal failure, and the blood urea commonly fluctuates between 50 and 150 mgm. per 100 c.cm. for years, occasionally rising in uræmic episodes to much higher figures. The inorganic blood phosphorus is raised, and may reach the dangerous levels of 10 to 15 mgm. per 100 c.cm. The calcium is lowered, and often clinical evidence of this may be found in a positive Chvostek sign or even in frank tetany.

FIG. 544.—RENAL DWARF OF NINE YEARS AND TEN MONTHS AND CONTROL SAME AGE.

FIG. 545.—SKIAGRAM SHOWING ATROPHIC TYPE OF RENAL RICKETS.

Note the thin cortex, well-marked rickets at the epiphyseal line, fracture of the shaft of the ulna, and general fragile, atrophic, and osteoporotic character of the bones.

(From *Archives of Disease in Childhood.*)

The radiological changes in the bones have been studied by Barber, Paterson, Parsons and others, and appear to be (1) actual cessation of growth and development at the epiphyseal line, (2) a rachitic change at the epiphyseal line, and (3) atrophy and osteoporosis of the bone (fig. 545).

Course and prognosis.—The course of the disease depends entirely on the form and progress of the underlying kidney disease and varies greatly. Some cases with a history denoting a congenital origin survive to early adult life, but when the bony deformities are clearly evident before the second year the patient rarely survives the age of five. Continual observation reveals that many cases pass into phases of temporary improvement in which the renal function recovers and the signs of the rickets temporarily disappear. The height of the blood urea gives little guidance in prognosis, but marked hypertension is an ominous sign.

Treatment.—A cure of the bone disease could only be affected by restoring the function of the kidneys. This might be possible in rare cases in which the renal disease was due to urinary obstruction capable of removal by operation, as, for example, in valvular obstruction of the posterior urethra. In the majority of cases the renal disease will run its appointed course. Large doses of natural or synthetic vitamin D may produce temporary improvement, but usually the greatest improvement will be achieved by giving a low phosphorus diet, with added calcium and alkalis.

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Fanconi syndrome

From the other varieties of renal dwarfism and rickets one form differs in ætiology and biochemical mechanism sufficiently to warrant separate description ; it is the form now known as the Fanconi, or de Toni-Fanconi, syndrome. It is a rare disease which may present at any age from infancy to adult life. Fundamentally it is a disorder of metabolism in which renal damage is a secondary effect. The renal pathology in the early stages is not clearly recognized, but autopsies on advanced cases have shown extensive destruction of renal parenchyma with scarring. Extensive deposits of cystine in the tissues have also been found at autopsy. The biochemical changes observed during life include aminoaciduria, glycosuria and systemic acidosis. In contrast to the other forms of renal rickets the blood phosphate is lowered rather than raised, and it is clear that the mechanism of production of rickets is quite different, and not nearly so well understood. Nitrogen retention occurs only in the terminal stages.

The presenting symptoms are usually bone pains and deformities,

though sometimes thirst and polyuria may be prominent symptoms. Radiology of the bones shows extensive rachitic changes, and these show little or no improvement with vitamin D therapy. It is usually at this stage that a renal origin for the rickets is suspected, and the finding of glycosuria on urine examination will suggest the diagnosis. Confirmation lies in the absence of evidence of nitrogen retention, the demonstration of excess of amino acids in the urine, and the presence of acidosis with a normal or low blood phosphate. Demonstration of cystine crystals in the bone marrow, or by slit-lamp examination in the eye, will add weight to the diagnosis. Treatment is unsatisfactory, but some improvement can be obtained by administration of alkalis.

For further information on this rare but interesting disease, and for discussion on its relationship to Lignac's disease (cystine storage disease) and to other forms of renal rickets, the reader is referred to the authors cited below.

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Lower nephron nephrosis

Reference has already been made to the syndrome characterized clinically by anuria and pathologically by degenerative changes in the epithelial cells of the distal convoluted tubules, to which the term " lower nephron nephrosis " has conveniently been applied. This form of renal damage occurs, not as a primary illness, but as a complication in the course of other illnesses, or of the therapy applied to them, notably after severe and prolonged crushing injuries, blackwater fever, sulphonamide therapy and incompatible blood transfusion. The first indication of the renal involvement is usually pain in the loins, followed by the passage of dark brown or black urine and then by anuria. The urine last passed contains albumin, cellular and granular casts and amorphous debris ; spectroscopic examination shows the presence of hæmoglobin or methæmoglobin. In many cases the anuria persists until death occurs quietly from uræmia several days from onset, but in less severe cases the flow of urine becomes restored after several days, and when recovery occurs it is complete. Treatment consists in attempting to maintain the water and electrolyte balance during the period of anuria, and avoiding diuretics and excess fluid intake ; it has been described in detail under the heading of " Anuria " (p. 1546).

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Nephrocalcinosis

The term nephrocalcinosis is here being used in a limited sense, not to include all cases of calcification in the kidney, but rather in reference to a clinical syndrome, known also as Lightwood's syndrome, of hyperchloræmic acidosis in which calcium deposits may be found in the distal renal tubules.

The disease is uncommon and is seen chiefly in infancy, although similar cases in adult life have been described by Albright. Either sex may be affected. The ætiology is unknown, though some cases appear to follow urinary infection, and Stansfeld (work to be published) believes that this is the usual cause. The anatomical changes found at autopsy,

FIG. 546.—RADIOGRAPH OF ABDOMEN OF BOY OF THREE YEARS WITH THIRST, POLYURIA, FAILURE TO THRIVE, ALKALINE URINE AND HYPERCHLORÆMIC ACIDOSIS.
The renal calcification is unusually heavy and coarse.

which are probably the result rather than the cause of the illness, are degenerative changes with calcification in and around the distal convoluted tubules of the kidneys. Burnard and Latner suggest that the primary functional defect is an inability of the proximal convoluted tubules to absorb bicarbonate. This results, on the one hand, in the passage of an alkaline urine, and, at the same time, in a retention of chloride and production of systemic acidosis. The excess alkalinity of the urine in the distal tubules leads to deposition of calcium and to damage to the tubular cells.

The first symptom, usually occurring during the early months of life, is failure to thrive, and this is accompanied by constipation and bouts of vomiting. Diarrhœa may complicate the picture, and lead to severe dehydration. There is a tendency for the infant's condition to fluctuate strikingly from day to day. There is usually anorexia, but thirst may be

a striking symptom. At times the air hunger of acidosis is very evident. The urine is increased in amount, and is persistently neutral or alkaline to litmus; in other respects routine examination of the urine shows very little amiss, though a trace of albumin and a few leucocytes may be present from time to time. Chemical examination of the blood shows a rise in chloride and a fall in alkali reserve. Except during periods of dehydration, the blood urea is normal. Radiology of the abdomen occasionally shows the presence of numerous minute calcium deposits in the renal areas (fig. 546), and rarely rachitic changes may be present in the bones.

The natural history is not fully understood, but it is known that recovery can occur, though many cases have died after an illness lasting several months.

The disease will be recognized if repeated specimens of urine are examined for *p*H (indicator papers are adequate for clinical purposes) in infants failing to thrive. The finding of a high blood chloride and low plasma bicarbonate with a normal blood urea will strongly support the diagnosis, and Latner suggests that the finding of a high partial pressure of carbon dioxide in the urine (above 50 mm. of mercury), collected by catheter under paraffin, will clinch the diagnosis.

The accepted treatment is the administration of alkalis in the form of Shohl's mixture (see p. 352) for prolonged periods, and in dosage sufficient to relieve symptoms. It is as yet too soon to say whether the use of streptomycin will prove as effective.

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Urinary infections

Probably most important of all illnesses affecting the urinary tract in childhood are the suppurative infections, commonly referred to as pyelitis or pyelo-nephritis. The frequency of these infections, either as apparently primary illnesses or as complications in the course of other diseases, is such as to demand a routine microscopic examination of the urine of any sick infant. Their importance lies not only in their frequency, but also in the severity of the acute illness and in the possibility of renal damage which may later ensue. The term pyelitis, used constantly by earlier writers, points to the original conception of the disease as an inflammation of the lining membrane of the renal pelves; but later investigations show that the inflammatory changes are seldom, if ever, confined to the mucosa, but involve the renal parenchyma, so that the term pyelo-nephritis is more appropriate. The inflammatory changes

may extend also to the urinary bladder, but cystitis as an isolated phenomenon is so rare in childhood that it will not be considered further in this chapter.

Ætiology.—No age is exempt, and urinary infection may occur in the neonate as in the older child, but the greatest incidence is between the third and ninth months of life, in the so-called "diaper age." A greater frequency in girls has given support to the view that infection is often ascending through the urethra; but in many cases the evidence points to blood-borne infection of the kidneys, and it remains undecided as to what proportion are the result of blood-borne infection, and what of ascending infection. It is known that transient bacteræmia is common, and that micro-organisms can be excreted by healthy kidneys. It seems likely that in conditions of lowered resistance these organisms may gain a foothold and lead to inflammatory changes in the kidneys and urinary tract. The phenomenon of infection following obstruction in a hollow viscus is well recognized, and the occurrence of chronic or recurrent urinary infections in children with obstructive lesions in the ureters or urethra is to be expected. What is not so easy to understand is a similar liability to infections in children with other congenital anomalies of the urinary tract, such as duplex ureter, where no obstruction is apparent.

The organism most commonly found on culture of the urine in cases of urinary infection—in 92 per cent. of cases investigated by Kowitz—is the colon bacillus, but it is still undecided as to whether this organism is the primary cause of the illness or whether it is a secondary invader which outgrows the original infecting organism in the urine. Doubts on its claims are cast by the frequency with which cultures of this organism can be obtained from the urine of healthy children, and in cases of urinary infection apparently secondary to infection elsewhere with some other organism, *e.g.* a streptococcal infection of the middle ear. In a minority of cases of urinary infection some other organism—a staphylococcus, streptococcus, B. proteus or B. pyocyaneus—may be cultured from the urine. The organisms so often seen on direct microscopy of urine which has stood for a short while are commonly contaminants.

Pathology.—When death is due to the disease, a focal suppurative interstitial nephritis with some pyelitis is found. There is a great technical difficulty in determining if such a condition as pyelitis without changes in the kidney ever exists. Unless the post-mortem examination is performed immediately after death, the urine destroys the lining mucous membrane. No doubt this led many of the earlier observers astray. Some hold the view that simple pyelitis exists, but death does not occur unless a pyelo-nephritis ensues. On the other hand, we have evidence that recovery from a pyelo-nephritis is possible, and that cases of pyuria, which have been diagnosed "mild pyelitis" and die from another cause, may show no lesions at all. Chown examined the post-mortem material from thirty cases of infants in whom the diagnosis of pyelitis, pyelo-nephritis or pyelo-cystitis had been made before death; twenty-one of these had well-marked lesions in the kidney with only slight changes in the pelves; four had no lesions which could account for the pyuria;

one had kidney lesions which were in the process of healing. The changes in the bladder were insignificant.

Recurrent or chronic pyelo-nephritis leads to permanent structural damage to the kidney, already described in connection with chronic Bright's disease with uræmia and hypertension, and renal rickets.

Symptoms.—The severity of the illness differs in individual cases, and the clinical picture may vary from that of the intoxication of an acute infectious disease to that of symptomless pyuria. For purposes of description, cases can be divided into the acute urinary infections of infancy, acute urinary infections of later childhood, chronic and recurrent urinary infections, and the late results of urinary infections.

Acute urinary infections of infancy form the most common group. The illness is characterized by severe constitutional disturbance without any symptoms localizing the condition in the urinary tract. The onset is usually sudden with high fever, and within a few hours the infant gives the impression of being seriously ill. Convulsions and vomiting and even rigors may occur at this stage. The fever continues and within a day or two there ensues a state of wakeful misery, restlessness and pallor which suggests the diagnosis to the experienced observer. Meningitis or pneumonia may be suspected, but the apathetic somnolence of the one and the dyspnœic contentment of the other are quite unlike the picture of pyelitis. The child, usually lying on her back, with eyes wide open and bright, remains fretful with frequent cries or shrieks. Little can be done to comfort her. She cries and is willing to drink, grasping the bottle greedily only to push it away after a few swallows. The fever is remittent, reaching 104° or 105° F., but mild cases occur with a temperature about 100°; and septic cases with a high swinging temperature reaching 106°.

Physical examination of the infant reveals no localizing signs, and the urine may appear clear or slightly cloudy, but microscopic examination will reveal the presence of numerous leucocytes.

In the absence of treatment the course of the illness in infants with normal urinary tracts is usually towards recovery in a period of weeks, though full return to health is gradual. With efficient treatment, recovery is usually a matter of a few days. At times a particularly severe form of urinary infection is seen in which malnutrition and anæmia develop very rapidly. It is often associated with gastro-intestinal disturbances, and jaundice may develop as a complication. The mortality is high, and autopsy reveals extensive pyelo-nephritis. It is probable that a colon bacillus is truly responsible for this form as this organism may be cultured from the blood as well as the urine.

When acute urinary infection complicates some other illness, such as pyloric stenosis, it may manifest itself only by deterioration in the infant's condition together with fever, and the diagnosis will be passed over unless microscopic examination of the urine is performed.

Acute urinary infection in later childhood has a much greater tendency to present itself as a urinary disease than in infancy; the constitutional symptoms are commonly less severe while the local symptoms are more prominent. Even so, puzzling cases occur, in which diagnosis may be

obscure for a few days. The most common sequence of events is that the illness starts with a fever, headache, malaise, irritability and pain in the back, and for a few days resembles an influenzal attack or even a paratyphoid infection. Then it is noticed that there is a constant desire to pass water, or that the pain is becoming more definitely localized in the loins and lower abdomen, and pus cells and bacilli begin to appear in large numbers in the urine. With adequate treatment, recovery is rapid. There are other cases of acute urinary infection of a more severe character which start suddenly with vomiting and high fever, without any immediate urinary signs. Seen on the second or third day of the illness they look flushed and intoxicated and there is an increased respiratory rate due probably to acidosis. Examination of the lungs often suggests diminished air entry at the right base, and this may lead the unwary to diagnose lobar pneumonia. Sometimes there is definite abdominal pain and apparent tenderness in this type of case, and the illness is liable to be mistaken for appendicitis. It must be pointed out that in about 10 per cent. of cases of acute appendicitis pus cells are present in moderate numbers in the urine, so that, if the symptoms point to appendicitis rather than urinary infection, laparotomy is advisable even though pus cells are present in the urine.

Chronic and recurrent urinary infection in infancy usually produces a characteristic clinical picture. The infant is brought for advice on account of recurrent vomiting and failure to thrive, together with anorexia and irritability. Examination reveals a restless, miserable, wasted infant, with sallow, lax, dry skin. There is usually a little fever. Nothing on physical examination would lead the uninitiated to suspect urinary disease. The condition of the urine is extremely variable; in some cases there is sufficient pus to form a heavy deposit in the bottom of the glass, while in others only a few pus cells may be found on microscopic examination. Indeed, it may be necessary on occasion to examine several specimens before any pus cells are found. Without treatment the illness may last for several months, and even with effective treatment there is a great tendency to recurrence.

In older children chronic urinary infection presents with frequency of micturition, enuresis and general ill health.

The late results of urinary infection have already been mentioned, and it is necessary here only to repeat that chronic or recurrent urinary infection may lead to extensive damage to the renal parenchyma with scarring, and that this may later produce the picture of chronic Bright's disease with uræmia and hypertension, or of renal rickets. Hence, it is important that early diagnosis of urinary infection in infancy should be sought, and that treatment should be effective.

Diagnosis.—In the older child urinary symptoms—frequency and pain—will usually lead to a correct diagnosis of urinary infection, confirmed by microscopic examination of the urine; only occasionally will difficulties in diagnosis arise as between urinary infections and pneumonia or acute abdominal emergencies. In the young infant, on the contrary, urinary symptoms are significantly absent, and correct diagnosis will be

made only by observation of the golden rule that in any sick infant microscopic examination of the urine is desirable; this desirability becomes a necessity in acute unexplained febrile illnesses, and in the syndrome of vomiting and wasting.

Treatment. The essence of treatment or urinary infections in infancy and childhood lies in the effective use of the sulphonamides, antibiotics and occasionally of the older urinary antiseptics (see p. 1540). It is often stated that, owing to the high concentration of sulphonamides which occurs in the urine, smaller doses of sulphonamides than those used for systemic infections are adequate to sterilize the urine; but the aim of treatment is not merely to sterilize the urine but also to eradicate infection from the renal tissues, and for this purpose it seems logical that the same dosage of sulphonamide should be given as for other systemic infections.

When, in a young infant, a diagnosis of acute urinary infection has been made, the first step consists in the administration of a full course of sulphonamide—we have a personal preference for sulphadimidine. Usually no other treatment is necessary. Symptoms abate in from twenty-four to forty-eight hours, and examination of the urine at the end of a week shows the virtual disappearance of the pus cells. Treatment can be stopped at this stage, but a further specimen of urine should be examined a fortnight later, to ensure that there has been no recurrence. When patients are treated in hospital more frequent urine examinations will naturally be made, but it is felt that the majority of acute urinary infections in infancy can well be treated in the home, and that this simple regime does not demand too much of the general practitioner. At times the illness is much more serious, and the severity of the vomiting renders the infant dehydrated, and at the same time prohibits administration of sulphonamide by mouth. In these instances admission to hospital is essential, and the administration of intravenous fluid by drip will be required. Once dehydration has been corrected sufficiently to promote a normal urine flow sulphonamide can be given in the intravenous fluid until such time as oral administration becomes practicable. When the infant fails to respond to sulphonamide a catheter specimen of urine should be cultured and the sensitivities of the infecting organisms determined, so that the appropriate antibiotic can be substituted for sulphonamide.

In cases of chronic urinary infection in infancy, initial treatment is on the same lines as those described, except that it is wise to continue the chemotherapy for a fortnight. If this fails to eradicate the infection, or if apparent cure is followed by relapse, a careful search should be made for any anatomical abnormality or evidence of urinary obstruction, using the techniques of radiography, excretion or retrograde urography and cystoscopy, and any underlying fault corrected surgically if this be possible. Otherwise, prolonged courses of sulphonamide or of the older urinary antiseptics should be given.

The same therapeutic attack is carried out in cases of urinary infection in older children, but here it is necessary to specify that the child should be in bed during treatment, and that fluids by mouth should be pushed, and combined with alkalis (see p. 1540).

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CHAPTER XXXIII

SURGERY OF THE URO-GENITAL SYSTEM

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UROLOGICAL INVESTIGATION

No branch of pædiatrics has witnessed a greater advance in recent years than that which is concerned with urology. Innumerable children have good cause to be grateful to pioneers such as Meredith Campbell in New York, Addison in London and Duncan Morison in Edinburgh. Their efforts, aided by the skill of the instrument maker and the radiologist, not to mention the bacteriologist and pathologist, have made possible the investigation of urological disorders in childhood along modern scientific lines. A wealth of accurate information and experience has been already garnered and is being daily added to in a field, previously uncharted, with correspondingly gratifying results in treatment. There are still technical difficulties to be overcome, and plenty of problems to be solved, but everyone must be thankful for the knowledge already gained and confident of further advances in the future.

The physician may call upon his surgical colleague for help in the following :

(1) Persistent or recurrent urinary tract infections.
(2) Gross pyuria with or without infection.
(3) Hæmaturia.
(4) Disorders of micturition (enuresis, dysuria, etc.).
(5) Pain of possible urinary tract origin.
(6) Tumours.
(7) Possible injury.
(8) Maldevelopment.
(9) Hypertension.

The information to be afforded by a complete urological investigation in such circumstances is usually essential to accurate diagnosis and effective treatment.

Procedure.—A careful enquiry into the history of the disorder, and a meticulous clinical examination should always precede any special urological manœuvres. The facts thereby elicited will often be found to indicate a diagnosis, and the subsequent technical investigations to establish it will be simplified.

History.—Whenever possible the child should be encouraged to tell his (or her) own story. Information is sought as to the duration, character, location and severity of pain, whether this is accompanied by fever, vomiting and so on. What are the urinary symptoms ?—frequency—urgency—wetting—scalding pain—difficulty in passing—any notable changes in the urine passed—quantity—smell—cloudiness or discoloration—whether any swelling or local tenderness has been observed. Thirst

and polyuria are significant of serious renal deficiency. Details should be taken of any previous or associated illnesses which may have a bearing, as well as any possible relevant points in the family history.

EXAMINATION.—A comprehensive clinical examination of the child follows. The general appearance as to colour, type and temperament, development and state of nutrition is noted. As a general rule it is surprising to find how little affected a child's general condition may be by quite advanced urinary disease. On the other hand, renal deficiency may be indicated by a sallow skin and a degree of emaciation and underdevelopment, which is characteristic. In its extreme form, it is often associated with skeletal deformities such as genu valgum (" renal rickets ") and with dwarfing (" renal dwarfism "). It is always well to estimate the child's height and weight in relation to its age.

The mouth, throat, nose and ears should be carefully inspected. Any focus of infection revealed may well be of importance. It is quite certain, for example, that a smouldering tonsillar disease can adversely influence a urinary tract infection. A relationship between an attack of acute tonsillitis and a recrudescence of a pyuria is frequently seen. Appropriate treatment must be instituted. The circulatory, respiratory and nervous systems must all be looked into. The blood pressure should be recorded and blood count, hæmoglobin percentage and sedimentation rate estimated. An investigation of the blood urea is always necessary. The lungs are carefully examined and an X-ray examination of the chest made if need be.

Various disorders of micturition, enuresis and so forth may have their origin in the central nervous system. Any degree of mental defect must be observed and the question of spina bifida and peripheral nerve lesions investigated (see later).

Finally comes the examination of the abdomen and external genitalia. Abnormalities of contour suggesting a renal swelling or distension of the urinary bladder are noted. The kidneys are palpated bimanually. In most children the lower pole of the right kidney only can just be felt. Any undue renal enlargement or tenderness is noted. Deep palpation along the line of the ureter may elicit tenderness. In rare cases, a grossly enlarged and thickened ureter may be palpated abdominally. A stone in the pelvic ureter can occasionally be felt *per rectum*. A distended bladder forms a characteristic suprapubic tumour, but it should be noted that it may not always be symmetrically in the middle line, but is at times eccentric in position.

A close inspection is next made of the external genitalia. In the girl any signs of vulvitis or vulvo-vaginitis with discharge are sought for, and the external urethral meatus is examined.

In the boy, the position of the testicles is assessed and they are digitally examined for any abnormality, particularly in the epididymis or spermatic cord. If necessary a finger in the rectum elicits any thickening or tenderness in prostate or seminal vesicles. The penis is inspected particularly as to the condition of the prepuce and external meatus. A narrow or " pin hole " meatus is a not uncommon cause of urinary obstruction, whilst

meatal inflammation or ulceration is of special significance (see later). If a degree of hypospadias is discovered, the meatus will commonly be found of minute size, necessitating meatotomy.

It may be important, *e.g.* when a urethral obstruction is suspected, to watch the child micturate, and it may often be desirable to estimate the residual urine by catheterization after the child has voided.

An exhaustive urinalysis is made as a matter of course—" urinalysis is the keystone of urologic diagnosis " (Campbell). First an ordinary specimen is examined by the usual methods and any abnormality in appearance, smell, chemical constituents or deposit is noted. Sterile specimens are then obtained for laboratory purposes (further investigation and culture). These must be fresh, obtained with perfect aseptic technique, and their despatch to the laboratory must be prompt. " Clean " or catheter specimens must be taken with meticulous care.

In boys a " clean " specimen may suffice. The method is as follows :

The prepuce must be well retracted, otherwise preputial contamination is certain. The glans and meatus are then purified with an appropriate antiseptic solution (oxycyanide or cetavalon). The boy is told to pass urine, the first half ounce or so is discarded and the remainder passed direct into a sterile flask, which is then sealed with sterile wool. If a catheter is used, it should be of soft rubber and the urine first withdrawn should be similarly discarded, so that any possible contamination from urethral debris is first washed away.

In the girl a " catheter specimen " is essential.

It seldom presents difficulty, but cleansing of the vulva and urinary meatus with the antiseptic must be thorough, and it should be realized that the girl's urethra will even then almost certainly contain infective material of external origin. For this reason the first urine withdrawn should be discarded as before, and the specimen only collected after the catheter has been washed through in this way.

It is important to collect the entire contents of the bladder as thick and solid constituents—pus and so on—tend to settle on the base of the bladder, appearing only in quantity with the last of the urine. The collection of urine from infants may present difficulties. In most female infants catheters are passable. But if not, as in boys, a test-tube, applied with adhesive strapping, the limbs being restrained if need be, must be made to serve.

On occasion, the total urinary output has to be measured. This in infants demands the same test-tube service—in older children there is no difficulty. The total fluid intake must of course also be measured and the records kept for comparison.

Renal efficiency (see p. 139).—Estimation of the blood urea is the most generally useful measure of efficiency in practice. The urea concentration test is also of great value. The injection of dyes (phthaleine, indigo-carmine), injected during cystoscopy, serve to contrast the activity of the two kidneys. They may also be employed quantitatively. Excretion pyelography also gives an indication of function, both relative and absolute.

Radiography is the " indispensible adjunct in urologic investigation and diagnosis " (Campbell). By its aid, the anatomy and to some extent

the functioning of the urinary tract can be visualized, and deviations from the normal demonstrated in a manner essential to accurate diagnosis. The following have to be considered :—

(1) " Straight " X-ray photographs.
(2) Excretion or descending and retrograde urography.
(3) Cystography.
(4) Urethrography.

The anatomical and physiological conditions of childhood present peculiar

Fig. 547.—Excretion Pyelogram showing Dilatation of Right Ureter and early Hydronephrosis (Left side normal).

The patient, a boy aged six years, had suffered from attacks of abdominal pain and vomiting for three years. Appendicectomy had been performed without relief.

Treatment. The right lower ureter was exposed by open operation and found greatly thickened and stenosed at its lower end. The muscle was split and the vesical orifice dilated.

Result (follow-up for five years). No further symptoms.

difficulties, sometimes still insuperable, but these are being steadily surmounted by improving technique.

Excretion urography.—To obtain satisfactory results, the medium must be reliable and safe, the maximum degree of concentration must be ensured, and obscuring gas shadows in the intestine must be eliminated as far as possible. Many suitable proprietary media are now available, *e.g.* iodoxyl, diodone. The dose given is usually higher than that recommended by the manufacturers.

Preliminary dehydration is essential to assure adequate concentration

and clear skiagrams. Fluids are rigorously withheld for some hours before the examination, so that the child is dry-tongued and thirsty. Intestinal gas, always a nuisance, has become even more so under modern conditions, with the preponderance of starchy elements in the diet. Efforts to eliminate gas by aperients, enemata, preliminary pitressin injections and so forth are valueless. The elimination of excess of carbohydrate food for two or three days has helped, but generally speaking it is best to leave the child to its normal routine of diet and activity and to regard the question of gas as a matter of chance. Before the medium is injected a " straight " X-ray should always be taken. If too much gas is seen the procedure should be deferred.

In infancy, adequate concentration of the medium cannot be assured, and attempts at excretion urography are apt to disappoint before the age of twelve to eighteen months at the earliest. This is particularly unfortunate since retrograde pyelography—at any rate in male infants—may also be impossible. Moreover, the difficulties of introducing the medium into the circulation in these infants are great. The veins are so tiny that intravenous injection will often necessitate cutting down. This can rarely be justified. Attempts to introduce the medium perorally or by intramuscular injection, which would be ideal in very young children, have not in our hands as yet afforded very much encouragement. The younger the child, the more important is it that the preliminary dehydration should be pushed to the point of harshness. Compression of the abdomen by means of a pneumatic bag or even manually is helpful.

Finally the defective kidney will, of course, fail to concentrate the medium. In the graver degrees of renal inefficiency, pyelograms will prove unobtainable by the excretion method and it should certainly not be attempted in the presence of acute lesions, or if there is reason to fear that renal failure is pending.

In unilateral affections, the contrast between the " silent " kidney and its acting fellow affords evidence of great value, but demonstration of the structure of the kidney can only be elicited by the retrograde method. Excretory ureterograms may be deceptive, as a thin trickle of the medium may indicate little or no change in calibre, when in fact the ureter is greatly dilated. Retrograde distension of the ureter may be essential to demonstrate the degree of ureterectasis.

Retrograde urography.—By the introduction of a suitable opaque medium the dimensions and outline of (1) the urethra, (2) the bladder, (3) the ureter and renal pelvis may be demonstrated.

Anterior urethrography.—This has little practical application in childhood, but it may be used in cases of suspected stricture or diverticulum. In the neglected meatal stenosis, dilation of the urethra may be thus demonstrable, congenital strictures may be visualized and possible diverticula detected. An appropriate medium, *e.g.* iodoxyl, is introduced through a urethral syringe and the picture taken laterally, the legs flexed and extended respectively so as to keep the femora out of the way.

Cystography.—A cystogram and in particular a voiding cysto-urethrogram, may be expected to yield valuable information as to the condition

of the posterior urethra, the size, shape and positioning of the bladder, the presence of diverticula and ureteral reflux. When reflux into the ureter is extreme a complete picture of the ureter and the renal pelvis may be thus obtained.

The making of a cystogram is a simple procedure. No anæsthetic should be given. The child is made to empty the bladder and a soft rubber catheter is then passed with due aseptic precaution. The opaque medium is then injected gently and slowly until the child complains of fullness and the desire to void. The catheter is partially withdrawn and clipped. The pictures are then taken, artero-posterior, oblique and lateral as required. By tilting the child and taking further pictures, if necessary, ureteral reflux may be demonstrated. Iodoxyl, 75 per cent., 2 c.cm. in 6 to 8 oz. water, is usually employed, emptying the bladder when the picture has been taken. If thought desirable the bladder may then be washed out with normal saline.

Cystoscopy and retrograde pyelography.—Whilst in expert hands no urological instrumentation need be viewed with apprehension, in childhood such procedures should be confined to essentials. If a sufficiently accurate diagnosis can be made, and the correct treatment determined, by the methods already outlined, the passage of instruments may be unnecessary and will be avoided by the experienced surgeon. Thus, when excretory pyelography has demonstrated the nature and site of the lesion, and the combined investigations have satisfied us as to the presence and capacity of the remaining kidney, it may be unwise and superfluous to subject the child to cystoscopy and retrograde pyelography (*e.g.* in the presence of a renal tumour).

In general, children stand instrumentation well, provided extreme gentleness and delicacy are exercised. The responsibility for these procedures should only be accepted by the specially trained. Obvious difficulties are imposed by the calibre of the child's urethra. This, of course, especially applies to boys. In infant girls, there is no difficulty and ureteral catheterization is usually possible with the smallest single catheterizing instrument available to us (12 Charrière). In infant boys one can rarely pass this instrument before the twelfth month, and ureteral catheterization may not be possible before eighteen months to two years. Considerable variability is found, however, in the calibre of the male urethra in children. Sometimes in a boy of four or five the urethra will only accommodate the smallest instrument; conversely, in some quite young children a larger instrument passes readily.

Preliminaries (*anæsthetic, premedication, etc.*).—The general management of these children demands the same gentleness, understanding and tact as any other surgical undertaking. Few children fail to respond confidently to those who refuse ever to deceive, frighten or hurt them. The gift of handling children is reserved for those who see things through a child's eyes.

Before a cystoscopy plentiful drinks should be given, so as to ensure a free flow of urine during the examination; no other special preparation is necessary. In some older children of a calm temperament the examina-

tion may be carried through without an anæsthetic. Premedication alone (nembutal, paraldehyde, apoidin, etc.) has been unsatisfactory. The writer has no experience of caudal anæsthesia (injection into the sacral foramen) so strongly advocated by Meredith Campbell. General anæsthesia seems desirable in the vast majority of cystoscopies in children, preceded always by a mild narcotic such as pentobarbitone. The anæsthetic need not be unduly deep and is never required for long. It is true that there are certain draw-backs from the surgeon's angle, *e.g.* in estimating bladder distension, etc., and an insensitive child imposes an even sterner discipline upon his manipulations, since clumsiness can evoke no warning complaint, but despite all these disadvantages, general anæsthesia appears to be wise for the majority of children.

Position.—The child lies on its back, the legs abducted and slightly flexed at the hips. Simple leg pieces can be adjusted to fit the ordinary child's operating table and a sliding drip tray fixed under the table flange is useful.

Procedure.—The external genitals are carefully cleansed. Metal sounds are passed in sequence, beginning $\frac{7}{9} - \frac{13}{15}$. The external meatus is usually the narrowest spot in the urethra and may have to be nicked on the ventral side with scissors (meatotomy). It is preferable to avoid doing so at this moment if possible as the resulting drop or two of blood is apt to obscure the " window " of the instrument and be a nuisance.

The bladder is now washed out, using boracic lotion or saline, until the fluid returns clear, when it is filled with 2 to 6 ounces of the medium, according to age. This may be done through the cystoscope or by means of a catheter and syringe. There is much to be said in favour of the irrigating cystoscope, and it will doubtless become the routine instrument in children as in adults. But the syringe (8 oz. metal graduated) method is simple and efficient. Where the bladder holds much debris, cloudy or bloody urine, it is best to inject only 1 to 2 ounces at a time. Repeated small washes of this kind will be found more effective.

Once the bladder is well distended with the clear medium, inspection proceeds systematically in the usual manner. An underfilled bladder will look unduly red, suggesting inflammation, whilst the natural mucosal folds may be confusing. Conversely slight overfilling renders the mucosa unduly pale. The roof and walls of the bladder are rapidly inspected, and then the instrument turned so that the internal meatus can be viewed, and, from this, the trigone and ureteric openings. With the irrigating cysto-urethroscope, the prostatic urethra is ballooned and scrutinized by withdrawing the instrument. The contractions of the ureteric openings and the nature of the efflux are noted. Under general anæsthesia the contractions are sluggish. Indigo carmine 0·4 per cent. (1 c.cm.) may be injected intravenously, and the time taken for the dye to appear gives an index of renal capacity. This is of particular value in a suspected unilateral lesion. Normally the efflux is coloured three to four minutes following the injection.

The ureteric openings vary considerably in appearance, shape, and accessibility to catheterization. Not infrequently they are papilliform or

obscured by folds even in the normal bladder. In the presence of cystitis and œdema, they may defy location.

When inspection of the bladder has been completed, ureteral catheterization may be proceeded with if desired. As a rule the manœuvre is not difficult, but it may often be extremely so, and on occasion impossible, owing, for example, to œdema. At other times the catheter enters the ureter easily but it is held up at varying levels, by hitching in the mucosal folds and so on. The greatest difficulties arise in the inflamed

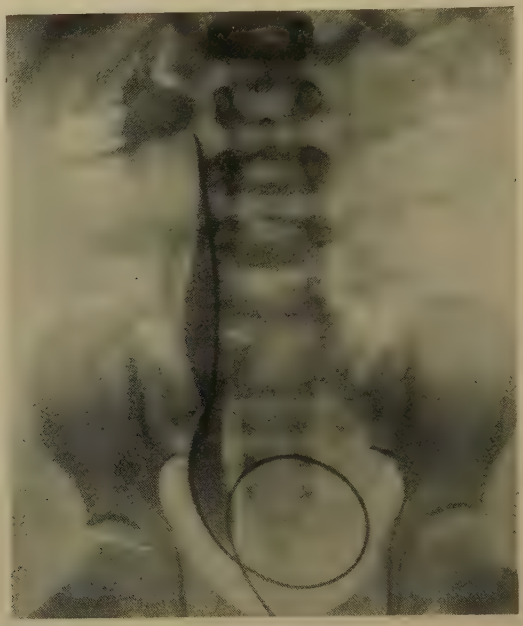

FIG. 548.—RETROGRADE PYELOGRAM SHOWING DILATATION AND SPASM OF THE RIGHT URETER FOLLOWING *B. COLI* INFECTION. LEFT URETER NORMAL BY EXCRETION PYELOGRAPHY.

The patient, a boy aged seven years, had suffered from intermittent attacks of abdominal pain for six months. Urine sterile on admission.

Treatment. Instrumental dilatation and Mist. pot. cit. and hyoscyamus.

Result. Cure after four weeks.

œdematous bladder. It is best to desist in such cases, giving the child a course of bladder washes before repeating the attempt.

Passing the catheter to the renal pelvis should be aimed at, and this should be done with care. It is quite possible to perforate the kidney. The writer has seen this mishap on two or three occasions. No ultimate harm resulted, but the possibility should be borne in mind.

When the catheterization is completed, the bladder is emptied and the cystoscope withdrawn. The catheters, marked R and L, are introduced into suitably stoppered test tubes for the collection of specimens and these are attached to the thighs. It is desirable to collect a c.cm.

or so of urine from either kidney. With the very fine catheters used (4, 5 F.) this is not always possible. If no drip materializes, a c.cm. or two of sterile saline may be introduced through a fine needle into the catheter and resuction may then start the flow.

Meanwhile any general anæsthetic is stopped, and the child moved to the X-ray room, which should be close by. When in position the opaque

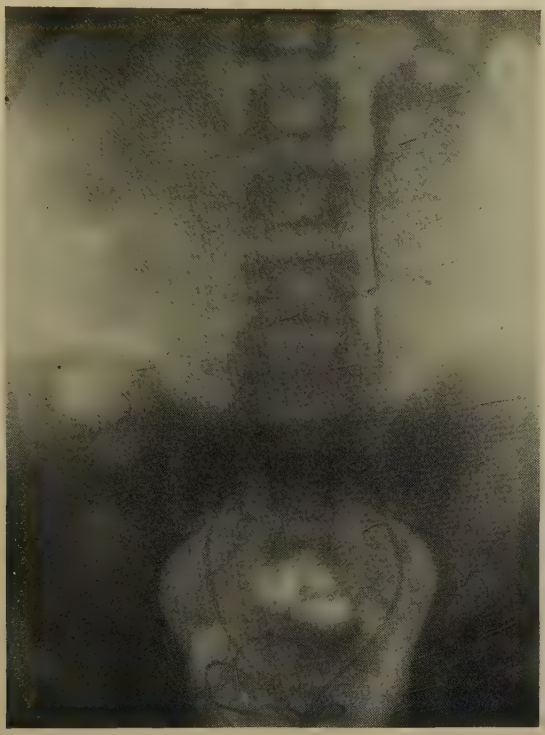

FIG. 549.—RETROGRADE PYELOGRAM SHOWING A LARGE HYDRONEPHROSIS OF THE RIGHT KIDNEY (LEFT SIDE NORMAL).

The patient, a boy of fourteen years, had suffered from attacks of right-sided abdominal pain and vomiting every three months or so since infancy. Appendicectomy had afforded no relief. At operation, the cause of the hydronephrosis was found to be an aberrant leash of vessels ; the kidney was, however, a mere shell and it was removed.

Result. No further symptoms.

medium is injected and the photographs taken. Sodium iodide solutions have now been entirely replaced by the preparations already mentioned.

The normal renal pelvis will contain approximately 1 c.cm. of fluid for each year of life up to the age of five or six. Accordingly 1 to 6 c.cm. are injected gently with a syringe. An exposure is then made, and the plate developed immediately, when it is seen whether enough solution has been used. If the pelvis is found to be enlarged, a further quantity of the solution estimated to be sufficient to fill the pelvis is

injected, and a second photograph taken. If the fluid is injected with care, over-distension of the pelvis will not occur, as the excess of fluid will escape down the ureter.

Hæmaturia of varying degree is very occasionally seen in the first specimen passed after the examination, but seldom later. It seems to be harmless. The catheters are withdrawn as soon as the pyelograms are known to be satisfactory.

DISORDERS OF THE EXTERNAL GENITAL ORGANS

The Prepuce

Phimosis.—The general medical attitude to the prepuce tends to be irrational and ill-advised, and the operation of circumcision too often inappropriately performed. However "vestigial" a structure may appear, some contemplation of its possible function should precede the decision to remove it.

Structure and physiology.—In the first place, every male infant is born with the "glans muzzled by the prepuce" (Bland-Sutton), and in the first week or two of life retraction is rarely possible. This arrangement is so constant that it must be the normal, and it is manifestly wrong to style it "phimosis." Moreover it is known that this normal close-fitting prepuce is, at birth, glued to the glans by adhesions of the congenital type—avascular, easily separated, absorbable and non-recurring. The effect is to cover the glans, and its sensitive vulnerable epithelium with a muco-cutaneous glove designed to "stay put" during the early days of life and only gradually to unfold to its full flexibility. The inference that this remarkably constant arrangement is meant to shield the glans from too early exposure is very strong. No one who has pondered the effects of ammoniacal dermatitis on the circumcised infant can doubt the protective value to the glans of its preputial covering.

But if a tight and virtually non-retractable prepuce is to be regarded as normal at birth, that is not to say that its persistence in this condition should be accepted as such. What of the subsequent development? It is obviously necessary that full retraction, permitting complete emergence of the glans and proper cleanliness, should ultimately be assured. Undoubtedly nature has her own orderly and unhurried plan for ensuring this, and it would be well to put some trust in the measures she has provided.

The normal activities of infancy increase the mobility of the prepuce. Infant nursing should include daily mobilizing from birth onwards as a normal routine. It is known that the adhesions tend to absorb quite early. Possibly the activities of the smegma glands may have a bearing. The secretion they produce during infancy is retained in the preputio-glandular sulcus. Its presence there causes no irritation to begin with; balanitis is practically unknown in infancy. Later, however, it may well, by doing so, further the completion of preputial mobility.

As the child and his penis grow, erections complete the stretching process, already well advanced, and the prepuce gradually assumes its relatively insignificant adult proportions.

In the writer's view then, Nature has thus planned the evolution of the prepuce to shield the glans until infancy is past, *i.e.* until bladder control is acquired, and diet is stabilized on adult lines. The story of ammoniacal dermatitis and meatal ulceration shows the wisdom of the plan, and the medical outlook should conform to it.

On the basis of such reasoning, the prepuce should not be expected to retract fully in infancy. It would be reasonable to expect to find partial retraction, enough to bring the tip of the glans with the external urinary meatus into view, becoming possible after the early weeks. Thereafter increased mobility may be looked for over the early years. But it should be regarded as normal for the glans to be out of view during these years.

There are of course many variations. The prepuce may be relatively long and loose, retracting early and easily, the so-called " redundant " prepuce ; it may be relatively short and tight, and retractibility delayed. But in the writer's view neither of these varieties calls for circumcision. If it is felt that retractability is unduly delayed, it may seem desirable to stretch the prepuce or better to enlarge the orifice by a dorsal slit, but even these procedures can be overdone. An anæsthetic should always be given. The dorsal slit is preferable because stretching with forceps can so easily be too forcible and lead later to contracture.

There will always, however, undoubtedly be some children in whom non-retractability persists, and in later childhood this undoubtedly calls for operative help : balanitis, *i.e.* sub-preputial suppuration may occur from retention of infective products in the preputio-glandular sulcus, and there is also the possibility of a paraphimosis : it is noteworthy that both these complications are practically only seen in older boys. Moreover, a phimosis persisting to adult life may well complicate, though it is more than doubtful whether it ever determines, venereal disease, and may undoubtedly predispose to cancer at a later age. These are not indications for circumcising every new-born male infant.

In older children then, a genuine phimosis may not infrequently necessitate a circumcision, but it is the writer's conviction that adequate early attention will greatly diminish the numbers.

In the light of the foregoing, the writer does not accept many of the " indications " commonly adduced for circumcision, as applied to infants. The operation is often recommended for the various forms of dysuria—for urinary obstruction, bed-wetting, etc., and to " reduce the strain " in infantile inguinal hernia. Dysuria with pain is most commonly caused by ammoniacal dermatitis, complicated by meatitis or ulceration. The prepuce is not the cause and is, in fact, a valuable asset. The prepuce is not a factor in causing enuresis, and it is practically certain that it is never a cause of urinary obstruction, though it may mask an all important " pin-hole " meatus ; it is not, therefore, an aggravating strain to a hernia. Circumcision is not justified for these conditions. Preputial

irritation is said to determine masturbation and to be an aggravating factor in certain neuro-muscular disorders, notably pyloric stenosis. These possibilities should not have any influence in a decision about operation.

Circumcision.—The indications for this operation are non-retractability of the prepuce after the age of infancy, paraphimosis, and recurring sub-preputial inflammation (balanitis) in older boys. The operation should be regarded as rarely necessary before the age of three years.

In regard to the operation, some points only call for observation here. The aim is to leave a readily retractile preputial fold, and the glans and preputial sac completely accessible, with the minimum of scarring and above all without interference with the highly sensitive frenal area. The line of removal should be oval, avoiding the frenum and deepening on the dorsal aspect; and the removal should be no more extensive than is necessary. The first dressing, *e.g.* flavine-paraffin ribbon gauze, should be replaced on the third day by powder—*e.g.* bismuth and iodoform.

"Napkin dermatitis" and "meatal ulcer."—This is an inflammatory syndrome, due to chemical irritation by ammonia, derived from the urine, manifested particularly during the napkin era, or in older children who suffer from incontinence of urine or enuresis. Hamilton and Middleton (1927) in an important communication summarized the existing knowledge of this condition and recorded valuable observations of their own. Zahorsky (1915) and later Brennerman (1921) had directed attention to the significance of the lesions and inferred a common origin. Cooke (1921) recorded his researches which established the causation of this clinical entity on a firm basis. Lanman (1924) later confirmed Cooke's findings.

Cooke proved the causal agent to be ammonia liberated from the urea of the urine "by the action of an intra-cellular urease present in a bacillus, which inhabits the colon in a large percentage of normal children." Cooke isolated this organism—*B. ammoniagenes*—and elucidated its peculiarities.

> "The bacillus flourishes best in a medium which is on the alkaline side of neutrality, while an acid environment causes cessation of growth. Thus, in the highly acid contents of the large intestine of the normal child the organism will not flourish. If the acidity be diminished it will begin to flourish, and will multiply the more actively, the nearer the reaction of the contents of the bowel tends towards alkalinity.
>
> Inoculated into a solution of urea, or into fresh sterile urine, under conditions favourable for its growth, it produces ammonia in considerable quantity in a very short space of time. It is the ammonia produced in this way in the urine-soaked napkin which is responsible for the irritation of the underlying area of skin."

Cooke demonstrated convincingly the reaction on the skin of his forearm. Clearly the chemical reaction of the contents of the large intestine is of great importance. So long as this remains acid, growth of the *B. ammoniagenes* is inhibited, and undue ammonia liberation is

prevented; conversely, diminished acidity encourages proliferation and a rising tide of ammonia.

The stools of breast-fed babies are known to be acid in reaction (Debré, Goiffon and Rochefrette, 1926), whereas in the bottle-fed, the stools become alkaline, approximating to those of the adult. Hamilton and Middleton emphasized this fact as explaining the rarity of ammoniacal dermatitis in breast-fed babies, and the frequency with which it is found to follow promptly on weaning. They further drew attention to recurrent attacks of excessive ammonia production, determined by flares in the bacterial activity, due to variations in the reactions of the stools brought about by changes in the diet and other factors. These " ammoniacal storms " are " accompanied by erythema or excoriation of the napkin area, and when the child passes urine through the irritated ring of skin at the tip of the prepuce, pain is caused and the infant screams." In the circumcised child a meatal ulcer is likely to develop. This irregularity of ammonia formation explains the late occurrence of meatal ulcer—it may be long after circumcision in many cases.

" The more ammonia there is liberated in the napkins, the more alkaline the contents of the napkin become and consequently the more rapidly does the offending bacillus proliferate. A vicious circle is initiated." So that " the intensity of the irritation is influenced by the length of time during which the napkins are allowed to be in contact with the child in a wet condition " (Cooke).

Clinical features.—The napkins smell strongly of fresh ammonia and " make the eyes run." The urine freshly collected is clear and free from odour. The " dermatitis " is confined to the napkin area and may show all degrees from a simple blush erythema to a scaly glazed epidermal thickening, blistering and ulceration, superadded infection may lead to severe ulceration.

The prepuce especially shares in the inflammation, becoming œdematous, scaly and possibly excoriated and even ulcerated at the tip. Retraction becomes impossible but there is no sub-preputial inflammation. The condition is not a " balanitis " as Hamilton and Middleton rightly insist—but a preputial dermatitis. It gives rise to much pain and difficulty in micturition, thereby aggravating the general misery and irritability of the child.

Meatal ulcer.—In the circumcised child, the unprotected glans and urinary meatus show analogous lesions. Patches are frequent on the glans and the meatus becomes inflamed, blistered and finally ulcerated. The lesion is superficial but exquisitely tender. Frequently a scab forms, temporarily blocking the orifice, and when this separates, there may be slight bleeding. The local and general disturbance is always severe. The child screams, and micturition is agonizingly painful and may be impossible until the scabs are softened. A drop or two of blood at the end of the act may add to the general alarm. The manifestations may in fact be so distressing as to suggest a serious lesion in the urinary tract.

The relation of meatal ulcer to contracture of the meatus is important.

It is common to find the lesion associated with a narrow meatus, requiring subsequent dilatation or meatotomy, but it is doubtful if the ulcer itself, which is quite superficial, often leads to contracture in healing, though possibly in some instances it may do so. In the girl the urethra is protected by its situation from these more disturbing complications.

TREATMENT.—" Napkin dermatitis " and meatal ulceration should be a rare affliction in infancy. It is discreditable that it is not so. The significance of breast feeding, and of a more intelligent and conservative attitude to circumcision, is clear. Orderly napkin routine and training, aiming at habitual dryness, are preventive measures of first importance. In the presence of the active lesions, the primary aim must be to keep the skin dry and thoroughly clean by frequent bathing, careful drying and napkin changing. Napkins should be carefully washed and rinsed to rid them of all traces of alkaline soap. Whenever possible all tight coverings are dispensed with and, in older children, a loose shirt only worn at night.

The " boracic acid method " as outlined by Hamilton and Middleton is most valuable. This consists of impregnating all clean napkins thoroughly with boracic powder before use and the use of this as a dusting powder. The mild acid deters the bacillus and counteracts the corrosive action of any ammonia formed. When effectively employed, the response is usually dramatic. Boracic ointment may be applied to the meatal ulcer and in older boys arranged by day on a lint square to prevent pressure and friction from the trousers.

Feeding must be regulated to promote complete digestion and alleviate any complicating enteritis. Apart from this, little can be effected on dietetic lines.

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THE VULVA

Vulval adhesions : " atresia."—This condition is not uncommon. The labia minora are fused together by a thin pellucid adhesion extending from urethra to perineum. Gentle separation of the labia majora puts this on the stretch, and demonstrates its delicate structure. A probe introduced at the upper end, splits the adhesion with ease and causes the child no discomfort, leaving only the merest suggestion of a raw surface. A little vaseline or boracic ointment should be applied and repeated daily for a week or so.

The origin of this adhesion is generally reputed to be inflammatory,

but it conforms more to the congenital type, resembling the preputio-glandular adhesion of the boy.

Vulvitis. Many small girls suffer from periodic redness and irritability of the parts about the vulval orifice, associated with a slight stickiness and unpleasant odour. The condition is usually quite superficial and the vagina unaffected. It often accompanies enuresis and mild infections of the urinary tract. The disappearance of the vulvitis coincides with the clearing of the urine and the disappearance of enuresis, so that the association is one of some importance. For treatment and for **Vulvo-vaginitis** see page 1666.

Injuries and foreign bodies.—Vulvo-vaginal injuries are occasionally met with from falls on splinters of wood and so on. Bleeding is apt to be profuse and alarming; I have never seen the urethra injured in a girl nor any perforation of bladder or peritoneum, but a careful inspection with a headlight should be made and any repair which seems desirable made without delay.

Foreign bodies—beads, shoe buttons, doll's eyes, stones and so on may be introduced into the vagina. Escape of evil smelling pus and some blood follow prolonged incarceration and should suggest the diagnosis. Removal presents no difficulty.

Hypospadias

In the male, the ventral wall of the urethra closes from behind forwards. Failure produces hypospadias, and the type and degree of the deformity depend upon the level at which development has been arrested. The deeper segment of the urethra is unaffected and bladder control is normal.

In the simplest variety the tube is complete to the base of the glans and the penis is well developed. The glans may or may not show a blind dimple at the site of the normal external urinary meatus. The prepuce, defective below, overhangs the glans—the characteristic "hooded appearance." This degree of hypospadias permits of normal urinary and sexual functions and calls for no attempt at plastic repair—unless for cosmetic reasons. As in all varieties of hypospadias, the terminal orifice of the urethra is often minute, and dilation or meatotomy may be required in infancy.

The other types of the deformity are more serious. In the penile variety, the urethra ends at some point on the penis, proximal to the glans. When the point of termination is far back it is called the peno-scrotal type, still further back—the perineo-scrotal. In all these the penis tends to be under developed and hooked over by fibrous bands on the ventral surface (chordee). The further back the urethra, the graver is the deformity.

Operative interference in the more severe types of hypospadias must not be postponed too long. If chordee is present the penis will not grow until it is freed, and for obvious psychological reasons urethral restoration should be completed before school days begin at, say, seven or eight years.

The current procedure is to plan stage (1) of the operation at about four years. In this the urethral orifice is freed and transposed backwards and all contraction bands are so dealt with that the penis can be straightened.

Stage (2)—refashioning of the urethra —is proceeded with two years or so later. The method of Denis Browne, by its operative simplicity, should now replace all the complicated operations of the past. It is a most gratifying procedure and gives satisfactory results in practised hands, and only experienced hands should attempt to deal with these grievous deformities.

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Ectopia Vesicæ and Epispadias

The incidence of ectopia vesicæ is happily low, 1 in 40,000–50,000 individuals (Campbell). This deformity results from arrested development of the ventral wall of the urogenital canal, resulting in failure of fusion in the middle line. If complete, the anterior wall of the bladder and corresponding part of the abdominal parietes are missing, the pubic bones are widely separated and the penis is cleft, so that the roofless urethra gapes widely (epispadias). The penis itself is short and bent upwards so that its dorsal surface rests on the pubic region. In the boy the scrotum is usually rudimentary, and the testes lodged in the inguinal region or completely retained. The umbilicus usually lies lower than normal. The extroverted bladder presents as a red protrusion and the papilliform urethral orifices are easily recognized by the periodic trickle of urine. As time goes on the constant wetting, inevitable infection, and ammoniacal decomposition, determine a degree of misery and degradation to which few bodily ills are comparable. The deformity does vary in degree. In some instances the splaying of the pubes is less severe, and there may even be a partially formed proximal urethra, as pointed out by A. R. Thompson (1937). In such cases restoration of the bladder neck is feasible and some encouraging success is now being achieved. In the worst cases with wide separation of the pubes, diversion of the urinary stream to the bowel by urethral transplantation is the only possible course.

Epispadias (cleft urethral roof) may exist with no corresponding outward defect of the bladder. It is generally held that complete incontinence is inevitably associated, but this is certainly not always so. I have seen occasional cases with some capacity to hold the urine.

In the girl an analogous urethral defect may easily pass for a time unrecognized.

A girl of seven sent to me for removal of tuberculous glands in the neck was stated incidentally to have been under treatment for enuresis since infancy. It was found that she was in fact completely incontinent, and that her urethra admitted the index finger with ease ! The lesion was a vesical neck ectopia (epispadias).

Treatment.—In epispadias and in selected cases of total ectopia an

attempt to restore a functional bladder may be made, but ureteral transplantation to the bowel and subsequent excision of the bladder affords the only reasonable prospect for most of the grievously afflicted children. The results justify the many risks involved. The operation should not be unduly postponed. It is quite feasible to transplant the ureters, usually one at a time at a fortnight's interval, at about the age of two years or even a little less.

The results of ureteral transplants by modern methods are not unworthy. The immediate operative risks have been largely countered. The incidence of subsequent ascending infection has been greatly reduced, and there is no doubt that a degree of urinary control can be looked for which will make life quite tolerable for the patient.

REFERENCE

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THE IMPERFECTLY DESCENDED TESTIS

There is still some conflict of opinion in regard to the diagnosis, prognosis and treatment of this condition.

Diagnosis.—The testis should be in the scrotum at birth but its absence therefrom is not necessarily abnormal. In the first place, complete descent may be delayed for a few weeks or even months. Then it is quite usual on occasion for testes to be retracted, when they may disappear from sight and touch into the inguinal canal. Such retraction does not constitute developmental abnormality. By extruding the testis and manipulating it gently towards its normal situation, it will be found to descend completely into the scrotum with ease. This is the so-called " retractile " testis. The parents can be completely reassured that no abnormality is present. When the testis cannot be fully brought down, " descent " is imperfect.

A variety of types and degrees are recognized.

(1) True ectopia. The testis has missed its way and assumed an erroneous lodging. Thus it may be in the perineum (perineal) in the upper thigh (crural) or even on the dorsum of the penis (penile). In such instances, the testis is usually of good size and development, and the cord of adequate length. Operative replacement in the scrotum presents no difficulty and the prognosis is excellent.

(2) Inguinal ectopia is by far the commonest type of developmental error. Here the testis, commonly of good size, though tending towards imperfect growth as can be noted in unilateral cases by comparing it with its normal fellow, has emerged from the external abdominal ring, and then turned upwards to lie in front of the external oblique aponeurosis ; the gland is therefore subcutaneous, and can be felt with ease, except in small fat children, when some slight difficulty may be experienced. In this type, the cord is always short, and it is impossible to manipulate the testis into the scrotum. Sometimes it may reach the upper scrotum, and, in that

event, complete descent at puberty is probable. But as a rule the inguinal ectopic testis demands appropriate treatment.

(3) Retained testis. In this type the gland is held up above the external ring, *i.e.* it lies permanently in the inguinal canal or higher, even within the abdomen. It tends to be small and ill developed, and the cord is of course correspondingly shortened. Again appropriate treatment is called for.

In a proportion of all cases a clinical hernia is present. The condition may be unilateral or bilateral.

Prognosis.—An answer is demanded to the following questions:

(1) If nothing is done, (*a*) What are the prospects of ultimate descent? (*b*) What if any are the risks incurred in having a permanent imperfectly descended testis?

(2) What is the value of hormone treatment?

(3) What are the results of operative treatment?

Every surgeon of experience has seen, occasionally, a held-up testis burst its bonds, and reach its appointed place in the scrotum at or about puberty. The writer has heard an eminent public school medical officer state that his records over twenty-five years show conclusively that every boy in his experience achieved this happy event before the age of seventeen. But it is quite certain that not all cases are so fortunate, for many adults are seen with undescended testes. Contrasting the incidence in boys and adults, Meredith Campbell concludes that natural descent occurs in two-thirds of the cases.

The obvious question follows, if some testes do descend naturally, should not all treatment be postponed until adolescence? The answer is that to do so risks the full function of the gland. If the testis is not in the scrotum at puberty, the spermatogenic function will never develop. Moore (1926) has shown that the temperature of the scrotum is slightly lower than that of the body, and this may be the determining factor in complete development.

Can the testis, brought down, *e.g.* by a successful orchidopexy, acquire the spermatogenic function? Yes, bilateral cases have proved functionally capable of procreation. What of the supposed "internal secretion" function? The evidence is that this is satisfactorily performed by the majority of imperfectly descended testes. In bilateral cases, even with abdominal retention (total cryptorchidism) the male characteristics as to voice and physique are rarely suppressed. These boys are, in fact, usually otherwise normal.

Risks in a testis remaining permanently undescended:

(i) Torsion. Undoubtedly such testes are liable to this urgent complication, as well as to strangulation of an associated hernia, though such events are comparatively uncommon.

(ii) Malignant disease. Bland-Sutton long ago drew attention to the incidence of malignancy in undescended testes. This is a serious risk and such growths, when seen, are appallingly deadly. The possibility constitutes an important factor in any consideration of treatment.

Hormone therapy.—The results have been disappointing. Pregnyl

has been mainly used; 500 international units at weekly intervals in six to twelve injections. In boys of the "Fröhlich" type, with small testes, improvement has been usually noted, with enlargement and often descent of the testes. But in all other cases, though the testis usually enlarged, descent did not follow. Moreover, the testis in some instances underwent subsequent shrinkage and fibrosis. For the common types of imperfectly descended testis, hormone therapy at present appears to offer no certain hope of cure, and does involve a risk of atrophy.

Operative treatment.—Orchidopexy to-day is a highly successful procedure. In experienced hands it is found possible to advance the cord sufficiently to place the testis in the scrotum and retain it there, with ultimate normal development in the great majority of cases.

To achieve this, a careful dissection of the elements of the cord, carried through with the utmost delicacy and meticulous hæmostasis is essential. The testicle and the spermatic cord are first isolated by division of all external adhesions. The vas and veins are then gently separated from their intimate peritoneal attachments. This involves the separation of the hernial sac, which is invariably present, although the pocket may only be insignificant. The vas and its vessels are then seen passing downwards into the pelvis and the spermatic veins coursing upwards to the renal area. The latter are always shortened by fascial bands. When these are divided with careful completeness high up in the retroperitoneal area, the cord instantly lengthens appreciably. The veins must, of course, on no account suffer the slightest injury. The edge of the fascia overlying the deep epigastric vessels is then divided so that these vessels are exposed. If necessary the tunica vaginalis is opened and the testis everted. Finally the gland is anchored suitably to the bottom of the scrotum and the stitch ensuring this anchorage is retained for two weeks, being fixed by elastoplast to the thigh, to prevent any upriding of the testis.

Delicate manipulation and unhurried hæmostasis do most to minimize the risk of scrotal hæmatoma. Replacement via the thigh (Torek) is rarely necessary in childhood, and should be reserved for the occasional case in which, after full dissection, the cord is found too short for immediate scrotal replacement. In general, however, when the cord is seriously short, it will be best to amputate the testis, at any rate in a unilateral case.

Age.—At what age should orchidopexy be done? It is held by some that the dissection is simplified in young children by the greater delicacy of the fascial tissues, and that the age of choice is round about the fourth year. The writer, however, believes that the operation can be carried through with more expedition and safety to the delicate structures of the cord when the child is older, and prefers seven to nine years as the period of choice. This ensures that the testicle will have settled down well before puberty changes may be expected to begin.

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Torsion of the Testis

Torsion may on very rare occasions occur in the normally descended organ. It is usually partial; if manipulative reduction fails, operation

must be undertaken without delay. Torsion of the imperfectly descended testis is more common, though still a rarity. The symptoms are acute, severe pain and vomiting, and the tense and tender lump simulates a strangulated hernia. The empty scrotum, however, gives the vital clue to the diagnosis. Prompt operation is necessary. If the testis is found to be still viable, immediate orchidopexy may be possible. More commonly orchidectomy is the only recourse.

Inflammation of the Testis—(Epididymitis—Orchitis)

The cause may be non-specific infection, mumps, tuberculosis or congenital syphilis. Injury may cause a temporary painful swelling of the testis. This is most often seen in the imperfectly descended organ, when it is an indication for early operation. Non-specific inflammations of the testis may be met with, especially in older boys, as a complication of a lurking basal cystitis. The lesion is primarily an epididymitis, and treatment must be aimed at the primary source of infection. In severe cases suppuration ensues and extensive destruction of the testis may result. In mumps, acute epididymo-orchitis is a serious complication, fortunately rare in childhood. It is more apt to occur when the primary salivary affection is slight, or even unnoticed, and especially in boys about puberty. The affected testicle is acutely swollen and painful, and there is accompanying fever and general malaise. The condition subsides after a few days, but atrophy commonly follows. Suppuration is rare.

Tuberculosis of the testicle

Tuberculosis of the testicle is more common in infants under two years than in older children. It often develops suddenly, and gives rise to swelling involving the body and epididymis. In other cases the process is more chronic, resembling that in the adult. The disease is more rapid in children, that is, softening and abscess formation take place more quickly than in the adult. Surgical treatment should be conservative. Abscesses may need drainage, and fistulæ curettage, but castration should be reserved for those cases in which the testis and epididymis are hopelessly diseased. The use of streptomycin (with para-aminosalicylic acid) and other antibiotics for secondary infection has greatly improved the outlook.

In *congenital syphilis*, both testicles are commonly affected, being usually small and stony hard.

New growths of the testicle

Malignant tumours of the testis are happily rare in childhood. Their histology is complex, but all authorities are agreed on the extreme degree of their malignancy. They are perhaps best classified as embryomas showing varying degrees of differentiation.

The sole clinical evidence in the early state is enlargement of the testis, which feels solid and heavy, though a coincident hydrocele may be present. The Aschheim-Zondek test is a valuable aid to diagnosis, and provides an index of success in treatment, since it will remain positive if metastases

are present. Early rapid and wide spread dissemination is the rule. The tumour should be handled little and gently and, in operative removal, the first step should be to sever the cord as high up as possible to minimize the danger of dissemination during the removal of the growth. Deep X-ray therapy may prove a valuable aid in treatment. A very rare neoplasm is the interstitial cell tumour associated with virilism.

Dermoid cysts of the testis have been described.

THE OVARY

Prolapse into hernial sac.—Not infrequently the ovary migrates into an inguinal sac in infants or little girls. It is readily recognized as a characteristically mobile nut-like body. Reduction is rarely possible without operation and there is considerable risk to the gland from attenuation of the blood supply. Operation should not be delayed. The ovary is restored to the abdominal cavity and the sac removed in the ordinary manner.

FIG. 550.—TUBO-OVARIAN TORSION.

Photograph shows right tubo-ovarian mass removed at operation from a baby girl aged two years and three months. The child had suffered acute abdominal symptoms—severe pain, vomiting and screaming attacks—for five days with intermissions. Definite tenderness developed in the lower abdomen, and a lump could be felt per rectum in the pouch of Douglas. Recovery uneventful.

Torsion.—Acute torsion of the tube and ovary can occur in little girls. The writer has operated on two cases. The symptoms are urgent, with severe pain of abrupt onset, and vomiting. The local signs are those of an acute abdominal lesion with hypogastric tenderness. On rectal examination in the writer's cases, a tender lump was palpable in the pouch of Douglas. The clinical picture suggests acute appendicitis, but the general toxæmia tends to be less. Operation reveals bloody serum in the peritoneal cavity and the blackened tubo-ovarian mass in the pelvis. Removal of this with a small drain for forty-eight hours ensures prompt recovery (fig. 550).

Ovarian cysts. Multilocular and dermoid cysts are met with now and then in older children, usually producing acute symptoms from torsion or inflammation (fig. 551 and 552). Removal presents no difficulties as a rule.

FIG. 551.—OVARIAN DERMOID REMOVED FROM A GIRL AGED FOUR YEARS.

The cyst was impacted in the pelvis and was causing abdominal pain, vomiting and some frequency of micturition. It could be felt above the pubes and per rectum. Recovery uneventful.

(Two-thirds natural size.)

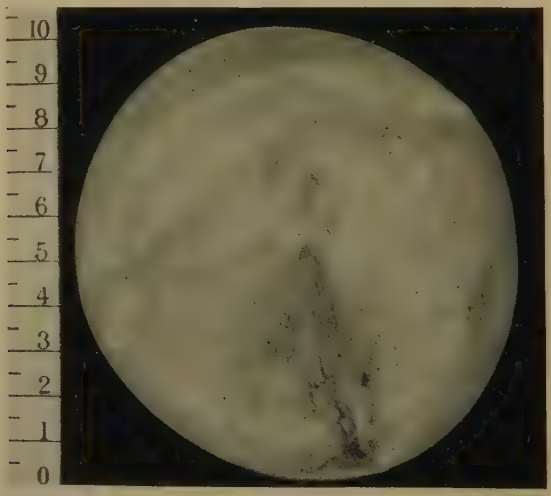

FIG. 552.—PHOTOGRAPH OF A REMARKABLE UNILOCULAR OVARIAN CYST REMOVED FROM AN INFANT GIRL AGED FOUR AND A HALF WEEKS.

There were no symptoms, but enormous abdominal enlargement. The pedicle sprang from the left ovary. Removal was simple, but the cyst had to be tapped during operation to facilitate delivery. It was therefore considerably larger than the photograph indicates (scale in inches). Recovery uneventful.

Tumours.—Sarcomata may present as large solid tumours in older girls. Those seen by the writer have been encapsulated, mobile, of awe-inspiring vascularity, yet so pedunculated as to make removal simple. The prognosis appears comparatively good.

THE URETHRA

(1) Female. The roof of the urethra may be developmentally incomplete (epispadias). The result is a patulous opening with complete incontinence (see p. 1600). Conversely, the urethral calibre is occasionally unduly narrow.

URETHRITIS. Some degree of urethritis often accompanies a vulvo-vaginitis and the shortness of the canal determines the frequency of an ascending cystitis in girls.

CARUNCLE.—True caruncle is rare, though vascular or angiomatous nodes are described as occurring, usually on the lower lip of the urethral orifice, sometimes tender, and commonly associated with enuresis. They are best destroyed with the electro-cautery. They must be distinguished from a pouting prolapse of the complete mucosal ring, which may occur in inflammatory lesions with severe straining.

(2) Male.—The boy's urethra is a potential field of intricate urological problems. Investigation may be carried out by urethrography, urethroscopy—anterior, by means of the irrigating urethroscope, posterior with the cysto-urethroscope. *Injuries*, and particularly rupture, require the surgeon's utmost skill, ingenuity and care if stricture is to be avoided. *Epispadias*, *hypospadias* and *meatal narrowing* have been dealt with elsewhere.

On rare occasions a *congenital* "*stricture*" of the penile urethra may aggravate a urinary infection and prohibit instrumentation. The calibre of the normal urethra in boys varies within wide limits. Fig. 553 illustrates reduplication—a very rare anomaly.

URETHRITIS—even gonococcal—is a possibility.

POSTERIOR URETHRA.—The verumontanum may be inflamed or hypertrophied, especially in association with excessive masturbation; resulting polypoid formations may be the causal factor of enuresis, and their removal be curative.

POSTERIOR URETHRAL AND VESICAL NECK OBSTRUCTION.—Under this comprehensive heading can be grouped an important series of cases, which have as their outstanding clinical feature an inability to empty the bladder normally. The disability varies in degree in accordance with the severity of the determining lesion, and is usually complicated, in the cases of long-standing, by chronic urinary infection. These cases are met with therefore in various forms. It may be as young infants, moribund from uræmia, as older children with constant urinary difficulties and general evidence of renal insufficiency, or as comparatively well-developed children with intractable enuresis or urinary infection. All depends upon the nature of the obstruction, but the essential effects

A

B

FIG. 553.—BIFID URETHRA WITH URETHRAL OBSTRUCTION IN BOY AGED EIGHT YEARS.

(*A*) Urethrogram shows the reduplication.

(*B*) Excretion pyelogram shows back pressure dilatation of bladder ureters and renal pelves.

of back pressure—retention, dilatation and renal destruction, aggravated, it may be, by infection—are, in some degree, common to all.

Elucidation and effective treatment offer perhaps the most difficult of all problems in children's urology. The cause of obstruction may be:

(1) Lesions of the posterior urethra { (*a*) Urethral "valves." (*b*) Enlarged verumontanum.

(2) Lesions of the vesical neck { (*a*) Sclerosis. (*b*) Neuro-muscular incoordination.

URETHRAL VALVES.—These anomalies are virtually confined to males, only one or two instances having been recorded in girls. Various types of valve have been described by Young. The rarest is that of an almost complete diaphragm stretched across the lumen of the urethra. More commonly bifid crescentic folds are found, running from the verumontanum to the lateral walls, partially fused and forming pockets, so that the emergent urinary channel is seriously narrowed, though an instrument passed from outside may encounter no serious obstruction. Secondary folds from the roof may further narrow the lumen (Sheldon, 1938). It is thought by some that these "valves" are in reality exaggerations of normal mucous folds in the presence of an underlying true urethral narrowing. There is, however, no doubt about the obstruction and its devastating effects. Even if the child survives to birth, early renal failure is to be expected. Of thirteen cases reported by Sheldon, ten died within a few weeks of birth. In occasional instances, however, where the obstruction is less severe, the child may survive longer, and, indeed, a number of instances have been recorded in adult, and even advanced, life.

In infancy, advice is usually sought on account of abdominal distension. This is due principally to the dilated bladder, though hydronephrotic kidneys may contribute to the general enlargement. As Sheldon has pointed out, bilateral hydronephrosis giving palpable swellings is more likely to be found in the "patients who die during infancy," than in older survivors. Dribbling incontinence by day and by night is also a constant symptom, although "this may not cause much comment in infants."

In older children, the history is usually of continued difficulties with micturition—wetting, frequency, dribbling incontinence and so on—by day and by night, together with poor appetite, occasional vomiting and general failure to thrive. Abdominal distension may have attracted attention. In the typical case, the child is undersized and sallow. The bladder is grossly distended, and the kidneys may be palpable. Asked to micturate, the child strains out a few scanty drops with much effort. A catheter usually passes easily and up to 15 or more ounces of residual urine may be recovered. It is usually wise to decompress the bladder very slowly leaving the catheter *in situ*, and allowing the urine to escape drop by drop. The blood urea is raised. It may be 90 to 100 mgm. per cent. or more, and the urine will almost certainly be infected.

Treatment.—Drainage of the bladder is the urgent need. Whenever

A

B

FIG. 554.—NOCTURNAL ENURESIS FOR THREE YEARS AND DIURNAL FREQUENCY IN BOY AGED SEVEN YEARS.

Urine moderate growth of staph. aureus. Bladder not distended. Residual urine 1 oz. Cystogram (*A*) shows dilatation of posterior urethra, reflux right ureter with diverticula. Excretion pyelogram (*B*) shows early hydronephrosis with clubbing of calyces. Cysto-urethroscopy showed pale hypertrophy of verumontanum. Improvement from urethral dilatation.

catheterization is possible, temporary decompression by this means is best, otherwise direct drainage by cystotomy (preferably by the introduction of a water-tight self-retaining catheter by the trocar and cannula technique) must be instituted at once. All general means available—drinks, infusions and so on—are then directed to the relief of renal strain. When the child's general condition permits, a more complete urological survey is made. Its purpose is to elucidate the site and nature of the obstruction, and to estimate the extent of renal damage. The diagnosis of a valvular obstruction is by no means easy, particularly in young children. A cystogram usually demonstrates dilatation of the posterior urethra, which shows a characteristic knob at the base of the vesical shadow. In bladder neck obstructions this is absent (see fig. 554). The nature of the lesion in the prostatic urethra, however, can only be determined by direct vision (urethroscopy). Destruction of the valve is of course the final objective. The ideal is electrosection through the cysto-urethroscope or division by a special punch. But retrograde passage of a bougie from the bladder has proved effective. More recently by using a retropubic approach, direct access to the urethra has permitted excision of the "valves."

Congenital enlargement of the verumontanum.—The obstruction is less in degree, and the clinical picture correspondingly less sombre. Enuresis and chronic infection are the predominant symptoms and it is in the course of investigation that the back-pressure effects, residual urine, vesical trabeculation, upper tract dilatation, etc., are revealed. The cystogram again shows the distension of the prostatic urethra, and on urethroscopy the hypertrophied verumontanum may be recognized.

Treatment is directed to reduction of the verumontanum either by dilatation or even diathermy.

Vesical neck obstructions.—In this group, the manifestations again are less urgent in type, urinary difficulties and infection predominating. Investigation reveals the same back pressure syndrome, but the prostatic urethra is not dilated and the cystogram is smoothly rounded off below. Sclerosis of the bladder neck (Young) may account for some of these cases. Some difficulty in the passage of instruments may suggest this. In others a "neuro-muscular" incoordination is surmised, but the precise explanation of this awaits further elucidation. Repeated dilatation helps to alleviate the condition. Spinal anæsthetics and injections of carbachol have been tried but have been unavailing in the writer's experience. In selected cases a wedge resection of the posterior lip of the internal meatus has proved a valuable procedure.

REFERENCE

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THE BLADDER

Cystitis.—A form of chemical or traumatic cystitis may result from drugs, either given by mouth or used locally as irrigation lotions, or from instrumentation or the introduction of foreign bodies. But in

general, cystitis is infective in origin, the organisms reaching the bladder via the urethra as, *e.g.* in vulvo-vaginitis, or from the kidney, *e.g.* in infective pyelo-nephritis, very rarely from an adjacent focus of suppuration, *e.g.* an appendicular abscess.

In *acute cystitis*, frequency, urgency, scalding pain and fever are distinctive features. Rest, local warmth, fluids in quantity, potassium citrate and hyoscyamus give rapid relief and, unless the primary infecting source remains active, may be expected to be curative. Thus the ascending infections associated with vulvo-vaginitis do not persist if the vulvo-vaginitis is cured. Where there is urinary stasis from a urethral obstruction, however, the cystitis is likely to be obstinate unless the obstruction can be relieved.

Chronic cystitis commonly follows renal infections. The cystoscopic appearances vary with the source and severity of the infection, from mere congestion to " bullous " or severe œdema, with clouds of debris and muco-pus. In ascending infections, the internal urinary meatus and adjacent vicinity appear worst. More often the changes will be most obvious around the orifice of one or both ureters indicating a descending infection. In the worst cases, identification of the ureteric orifices may be difficult and ureteral catheterization impossible.

Bladder lavage for a few days with boracic or oxycyanide lotions may simplify a subsequent cystoscopy. The treatment of chronic cystitis of this type is essentially the discovery and elimination of the primary focus (see p. 1627).

Urethro-trigonitis.—This lesion merits special mention. It is common in girls with enuresis, and may follow an infective cystitis or develop apparently insidiously, the urine remaining sterile. The appearances are those of intensive congestion of the vesical neck and internal urinary meatus sometimes with polypoid formation. Instillations of silver nitrate, 1 in 500, or even diathermy may be necessary to relieve the symptoms of vesical irritability. *Tuberculous cystitis* secondary to renal tuberculosis may be shown in the early stages by a wide spread patchy acute inflammation. More often the lesions are confined to the area around the ureter of the infected side which may itself show the well-known changes of rigidity and retraction (" golf hole "). Actual tubercles may be detectable in favourable cases. Later the typical shallow ulcers develop.

Non-specific ulceration.—Addison saw " two or three instances of a single ulcer in the floor of the bladder where there has been no bacillary infection or other cause found."

Fistulæ from osteomyelitis or tuberculous disease of the pelvic bones, or from intestinal infections, *e.g.* appendicitis, tuberculosis, actinomycosis may occur in almost any position, and show themselves on cystoscopy, as deep crimson areas of œdematous mucous membrane with a small dark hole or depression of varying size in the centre.

Diverticula.—These are rare in children, but may be the source of persisting infection. They occupy the usual situations in the base or lower lateral wall of the bladder, and are readily recognized on cystoscopy.

A special form is that seen not infrequently in which the ureteric opening is situated in a diverticulum. Ureteral catheterization in such cases is difficult. In extensive trabeculation of the bladder, which results from prolonged urethral obstruction, pouches between the trabeculæ may amount to "false diverticula"—but the size of the openings and the general appearances are quite distinctive.

Calculus (see p. 1630). Radiography usually detects the stone, though cystoscopy may be necessary (i) in the case of uric acid stone; or (ii) to determine the precise location. Thus stones impacted in the ureteric orifice or just above it may appear radiographically as in the bladder. There may be multiple stones, ureteric and vesical.

Ureteric calculus. Vesical manifestations.—Alterations in the appearance of the ureteric orifice vary according to the position of the calculus, and whether it is descending or fixed. With the calculus in the upper part of the ureter, changes in the appearance of the orifice are usually absent, though the rate of contraction may be altered. When the calculus is in the lower part, œdema of the orifice is frequent, and becomes more marked as the calculus descends. When the calculus reaches the intravesical portion of the ureter, the œdema becomes extreme, forming a great ring round the orifice, and spreading to the surrounding bladder wall. Hæmorrhages round the orifice are common. Owing to the œdema of its lips, the activity of the orifice is lessened, and its movements are sluggish. The frequency of contraction may either be increased or diminished, and, in the case of a calculus low down in the ureter, contractions may be absent.

In doubtful cases of ureteric calculus, X-ray pictures, both lateral and antero-posterior, should be taken with an opaque bougie in position. This procedure will probably settle the diagnosis. A catheter will usually be arrested by the calculus, but may pass it quite readily. A stone may be induced to pass by the injection through the catheter of 2 per cent. procaine, followed by liquid paraffin. A stone impacted in the orifice may be released by dividing the upper margin with a diathermy electrode.

Ureterocele (prolapse of the ureter).—In this condition the site of the orifice is occupied by a semi-translucent white or pinkish globe, on the surface of which blood vessels are seen. The minute opening of the ureter may be found somewhere on the summit of the cyst. The condition may be bilateral, and is due to a congenital narrowing of the orifice. Operation is called for to relieve the ureteric obstruction and ensure drainage.

Growths.—The writer has met with one large nævus of the bladder, which caused severe and prolonged hæmaturia. Transurethral diathermy failed to control the bleeding. Cystotomy and then electro-cautery proved completely successful.

A "myxoma" prolapsed through the urethra of an infant girl was removed by her doctor. The writer subsequently treated the small local recurrences seen on the base of the bladder by diathermy, and the child remains well (ten years).

Rhabdomyosarcoma ("sarcoma botryoides") or embryoma of the

uro-genital sinus is an exceedingly rare growth seen occasionally in childhood. It originates in the trigono-urethral area. In four patients under the writer's care, total cystectomy has been successfully performed. Three are well and one died six months after operation from mestastases. The papillomata of adults do not occur in childhood, though polypoid nævi described as such, are occasionally seen and are readily destroyed by the electro-cautery.

THE URETER

Congenital anomalies.—Much of the interest of urology in childhood centres around disorders of the ureter, and of these, developmental anomalies constitute a large proportion. In many instances both ureters are involved, and the kidneys may also share in the malformation, or suffer damage as a consequence of back pressure and infection.

FIG. 555.—PHOTOGRAPH (TWO-THIRDS NATURAL SIZE) OF THE RIGHT KIDNEY AND URETER, REMOVED FROM A GIRL AGED FIVE WEEKS.

The infant was admitted in a moribund condition but revived after blood transfusion. Pus was passed in quantity. Cystoscopy (1½ oz.) showed intense œdema of the right half of the bladder base, and pus could be squeezed from the right ureter. Left side normal. Right uretero-nephrectomy. The child made a good recovery and is now in excellent health.

The common presenting symptom is persistent or recurring pyuria, and the ureteral abnormality is revealed on urological investigation. Surgery, by means of instrumental or operative dilatation, or it may be by drainage or total extirpation of a disorganized focus of infection (nephrectomy, hemi-nephrectomy, nephro-ureterectomy), may contribute decisively to cure. Apart from very rare malformations, such as suppression or ectopic opening (into bladder, urethra or rectum) the anomalies of chief clinical importance are (1) dilatation without obstruction ("fœtal" ureter achalasia); (2) reduplication; and (3) stricture ureterocele.

(1) *Dilatation* ("*fœtal*" *ureter*).—The ureter is grossly dilated, and often redundantly convoluted. The vesical opening varies. It may be wide and patulous or diverticulous in type. Often it appears more or less normal. There is usually no obvious obstruction though the catheter may catch on mucosal folds. Valves have been described in some cases (Meredith Campbell). Often the renal pelvis shares in the dilatation and the condition is commonly bilateral—though usually more marked on one side.

Gross pyuria and febrile attacks often supervene, frequently in early infancy, and, in unilateral cases, extirpation of the uretero-renal pus sac may give gratifying results (fig. 555). In bilateral cases, if it can be established that the worse side is the aggravating focus, nephro-ureterectomy may still be justified, but in general, when the anomaly is bilateral, conservative treatment is alone possible.

(2) *Reduplication.*—The ureter may be double. Reduplication may be complete from kidney to bladder, with two renal pelves and two vesical openings; in this type the lower orifice in the bladder will be found to drain the upper renal pelvis, and the upper orifice to be that of the ureter from the lower half of the kidney. The two ureters in fact cross immediately above the bladder. The same arrangement may pertain on the opposite side and all four ureters may be catheterized. Bifid ureters may fuse at varying levels, most often at the vesical end, and open by a single orifice into the bladder. It is in such cases that obstruction of one and infection is most often seen. Extirpation of this ureter and the corresponding half of the kidney may then be feasible (fig. 556).

(3) *Congenital stricture* may accompany reduplication or be the sole lesion. The two common situations are the upper and lower ends of the ureters. Stricture of the upper end (uretero-pelvic junction) will determine a hydronephrosis. Stricture of the vesical opening is a common and important cause of ureteral dilatation and persistent pyuria. The contracted vesical orifice may be hidden in a diverticulum, which is misleading at cystoscopy, until the attempt is made to pass the ureteric catheter. In other cases, the ureteral mucosa prolapses, and cystoscopy reveals a ureterocele on the surface of which the contracted orifice may be visible. The treatment is to dilate the ureteric opening by the most appropriate method—bougies, electrosection, or if need be by open operation. It is usually necessary to open the bladder and excise a ureterocele.

The normal ureter in infections.—A severe infection of the urinary tract may be expected to lead to profound disturbance of ureteric function, especially in very young children. Œdema and spasm must tend to stasis and persistence of the infection (see infections of the urinary tract, p. 1624). Chronicity of such a state of affairs leads to degenerative changes in the ureteral wall, and ultimately to acquired dilatation (ureterectasis). Even when the urine has become clear and sterile, spasm and painful symptoms may persist (" ureteritis ") a clinical entity of considerable importance, since it may simulate, *e.g.* appendicular colic. It should be a cardinal rule in any child with unexplained colicky abdominal pain, to defer diagnosis until the results of a comprehensive urological investigation are available (fig. 557).

A

FIG. 556.—REDUPLICATION OF KIDNEY AND URETER ; CHRONIC INFECTION ; NEPHRO-URETERECTOMY IN GIRL AGED FIVE YEARS.

Intermittent febrile attacks with pyuria for two years. (*A*) Retrograde pyelogram. Right side one ureter and corresponding pelvis only filled. (*B*) Reflux ureterogram shows dilated ureter and right pelvis. At operation the upper half of the kidney and its ureter were virtually a pus sac. The lower half with its ureter appeared of good quality. Heminephrectomy was not, however, considered possible and total removal was performed. (*C*) shows specimen. Result : cure.

B

C

FIG. 556 (*see opposite page*).

A

B

FIG. 557. PYELOGRAMS (EXCRETION AND RETROGRADE) SHOWING URETERECTASIS IN A CHILD AGED SEVEN YEARS FROM PERSISTING INFECTION AND SPASM.

This girl had suffered from enuresis for three years following an attack of "pyelitis," the urine remaining mildly infected (enterococci and *B. coli*). Following dilatation of ureteric orifice through a cystoscope, frequency and wetting ceased and urine became sterile.

THE KIDNEYS

CONGENITAL ANOMALIES

Fœtal lobulation and undue length of the kidney are unlikely to be of clinical importance. Reduplication probably seldom causes any interference with health though, on occasion, stasis and infection may occur, and this is especially likely when the malformation involves the ureter (*q.v.*). Suppression only assumes importance if the solitary kidney becomes diseased, when the results may be disastrous. Fusion (horse-

FIG. 558.—HYDRONEPHROSIS IN A "HORSE-SHOE" KIDNEY IN MALE AGED EIGHT YEARS.

The boy had suffered for some months from attacks of severe pain in the left upper abdomen and loin, with vomiting and prostration lasting two or three days. On admission, a soft swelling could be felt in the left renal area. Urine sterile. Blood urea 38 mgm. per cent. Pyelography revealed a fused kidney with marked dilatation of the left pelvis, less marked of right. At operation, a very large left hydronephrosis was found to be caused by an aberrant vessel and associated adhesions. The vessel was divided, the adhesions cleared. The pelvis emptied at once. Operation completed by partial pyelectomy. Result (seven years): no further pain or urinary symptoms.

shoe kidney) or misplacement invites clinical complications—hydronephrosis, etc., and effective treatment may tax the surgeon's skill to the utmost (fig. 558).

Hydronephrosis

Dilatation of the renal pelvis may be primary or secondary.

(1) Primary. Congenital enlargement and malformation of the pelvis often accompanies the corresponding redundancy of the ureters

Fig. 559. Retrograde Pyelogram showing Clubbing of Calyces of Left Kidney due to Calyco-pelvic Spasm.

The girl, aged six, complained of aching pain in the left loin and there had been transient urinary infection (*B. coli*). Instrumentation and an antispasmodic mixture resulted in speedy cure.

("fœtal ureter," *q.v.*). The stasis and infection so likely to ensue, naturally aggravates the hydronephrosis. The condition tends to be bilateral. The treatment is as outlined (p. 1621).

(2) Secondary dilatation of the normal pelvis follows obstruction, whatever the type. Subvesical or distal urethral obstruction, unless it

is relieved, eventually brings about hydronephrosis and renal destruction by compression, but this section is primarily concerned with hydronephrosis resulting from obstruction in more intimate relation to the kidney itself. Commonly the affection is one-sided and the usual site of the block is the ureteropelvic junction.

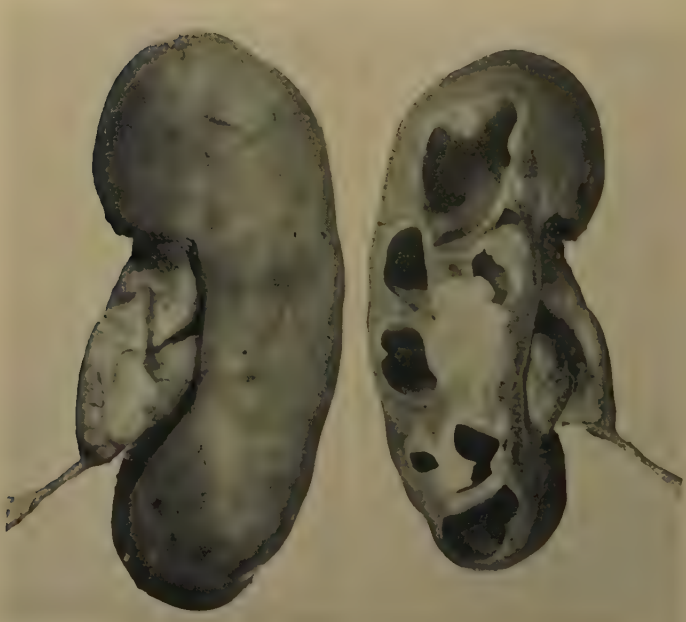
The causes are : (i) Stricture, usually organic narrowing of the ureteropelvic junction of congenital origin. Spasmodic contracture must be accepted as a possibility. Fig. 559 illustrates the earliest form—dilatation of the calyces, shown by clubbing in the pyelogram –presumably due to spasm of the spiral calycine muscles. (ii) Valves. The writer has seen one instance of valvular blockage of the uretero-pelvic junction. (iii) External adhesions. Perhaps the commonest factor often associated with congenital narrowing. (iv) Aberrant vessels, running to the lower pole, hitching round the ureter and holding it sling-wise. The vessels are usually associated with bands of connective tissue, but these differ completely in character from the denser adhesions mentioned in iii. The degree of obstruction produced varies and differing clinical pictures are thereby determined. Complete obstruction leads to rapid disorganization and destruction of the kidney. The result is a thin walled sac distended with attenuated pale or colourless urine. This type presents as a large cystic tumour often in early infancy, indeed it may be present at birth and complicate delivery. Removal is usually simple and, provided the remaining kidney is normal, all will be well. In the majority of cases, however, the obstruction is incomplete, and the disintegration of the kidney more gradual.

This latent or intermittent type of hydronephrosis is of great clinical interest and importance, and may come to notice in various ways. Thus it may be brought to light as the cause of a persistent or recurrent pyuria ; or may present as an abdominal or loin tumour. Perhaps most important of all are those cases, characterized by critical attacks of pain of abdominal type and vomiting. The condition may easily be mistaken for an acute abdominal lesion, *e.g.* appendicitis. At the height of the attack, the tense kidney may form a detectable tumour, and successful ureteric catheterization will drain the hydronephrosis, giving prompt relief. But often the symptoms are less dramatic and more transient, and the signs indefinite. In the most advanced cases, the affected kidney may be completely " silent " to excretion pyelography. Cystoscopy confirms delayed or absent excretion of dye from the hydronephrotic kidney. If the ureteric catheter can be induced to enter the sac free flow of a paler urine is characteristic and a large hydronephrosis may be emptied in this way.

The main value of urological investigation is to prove the quality of the remaining kidney, an essential preliminary to operation.

Treatment.—The treatment of a unilateral hydronephrosis is operative. The surgeon's aim is always to conserve the kidney if possible (fig. 560, 563). In practice this is often not feasible, and nephrectomy is the only resort. During recent years, out of a large series of cases the writer has carried out conservative procedures on some seventy cases.

A



B *C*

FIG. 560.—PYELOGRAMS AND OPERATION SPECIMENS FROM A GIRL AGED THREE WHO HAD SUFFERED FROM INCONTINENCE AND ABDOMINAL PAIN.

Urine heavily infected (*B. coli.*) Blood urea 50 mgm. per cent. Cystoscopy. Marked basal cystitis. Pyelograms show right hydronephrosis, uretero-pelvic stricture and dilated ureter. Left side normal. Right nephro-ureterectomy. Result: cure.

FIG. 561.—HYDRONEPHROSIS DUE TO ABERRANT VESSELS, WITH CALCULUS IN BOY AGED SEVEN YEARS.

History of "attacks of nephritis." On admission urine sterile. Excretion pyelogram shows hydronephrosis of the left kidney with a pelvic stone. At operation, the cause of the hydronephrosis was found to be a leash of aberrant vessels. The kidney was of good quality. The stone was removed, the vessels divided, and the kidney preserved. The boy has had no further trouble (8 years.)

FIG. 562.—POLYCYSTIC KIDNEY.

Of this number five have required subsequent nephrectomy. The remainder have shown a most encouraging absence of later trouble. The operative procedures have included division of aberrant vessels, adhesiolysis, plastic reconstitution of uretero-pelvic strictures, combined, when needed, with excision and reconstitution of the redundant pelvis. As already indicated, the writer feels strongly that, with earlier diagnosis, this field of conservative surgery could be appreciably widened (fig. 561).

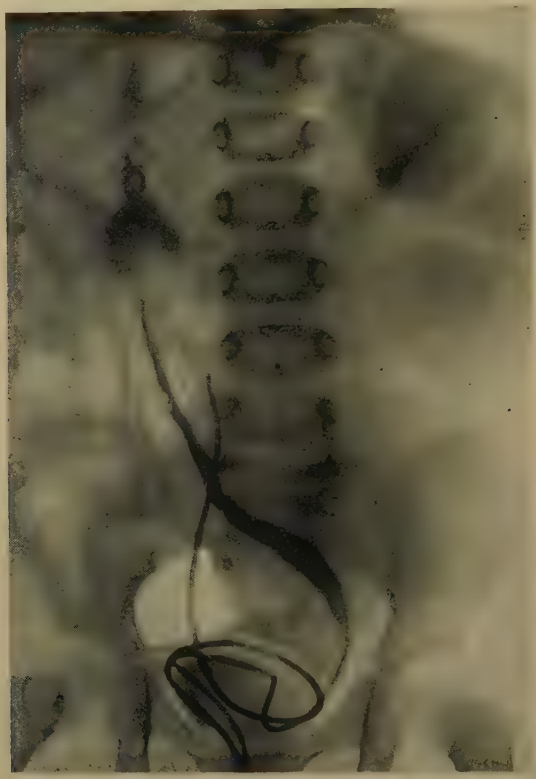


FIG. 563.—PYELOGRAM SHOWING LARGE LEFT HYDRONEPHROSIS (RIGHT SIDE NORMAL).

Child aged one year six months. Presented with acute abdominal symptoms—pain and vomiting. Soft cystic swelling in lower left loin and abdomen. Urine heavy growth (*B. coli*). Note displacement of right ureter across the middle line. This unusual feature was explained at operation when adhesions were found, binding the lower pole to the opposite kidney area (partial fused kidney). (Hydronephrosis due to uretero-pelvic stricture.) Following nephrectomy recovery uneventful, and urine speedily became sterile.

URINARY INFECTION

Acute infections of the kidney.—Surgical intervention may be indicated when high fever persists for some days with tenderness, muscular rigidity and fullness localized to one renal area. This is especially so if

a tumour can be distinguished. The condition may be due to distension of the normal pelvis with purulent urine (acute hydronephrosis) from inflammatory ureteral obstruction, to infection of a pre-existent hydronephrosis, or to local suppuration in or around the kidney (pyonephrosis, perinephritic abscess, renal carbuncle.) A distended renal pelvis may be drained by the careful passage of a small-sized (4F) ureteral catheter, which may be left *in situ* for twenty-four to forty-eight hours. Immediate relief may be thus afforded, and on withdrawing the catheter, normal ureteral drainage usually ensues. If not, the manœuvre should be repeated.

The grosser suppurative lesions necessitate operative interference and, since a nephrectomy may be called for, it is essential to be assured first that the functional capacity of the other kidney is satisfactory. But these children are so gravely ill, that it will generally be found that the wisest course is to drain the abscess first and complete the operation when necessary at a later date.

Infected hydronephrosis. It frequently happens that an acute infection first draws attention to the existence of a hydronephrosis. Fever, pain and local tenderness are associated with a tumour often of large size in the loin. If ureteral catheter drainage can be achieved, valuable temporary relief may thus be given. The surgeon should temporize whenever possible, so that a deliberate operation can be planned when all the necessary evidence is available (see section on hydronephrosis). Frank suppuration is rare, but if the general appearances are too grave to warrant delay, simple drainage of the infected sac (nephrostomy) should be carried out through a loin incision.

Pyonephrosis.—Apart from multiple pyæmic abscesses, which are usually bilateral and rapidly fatal, a unilateral empyema of the kidney is occasionally met with in children. The condition follows on an acute pyelo-nephritis, and may be suspected when the acute stage persists with marked local signs (acute pyonephrosis). More often the acute phase subsides but the child remains obviously ill, sallow and anæmic, with a swinging temperature and a local tender lump in the renal area, with a functionally silent kidney. Drainage of the pus sac is urgently called for to minimize the danger to the opposite kidney. The affected kidney is certain to be completely disorganized, but its removal should not be contemplated until the child's general condition warrants. Subcapsular nephrectomy will then be found the method of choice.

The following cases, occurring under the author's care, illustrate well the chronicity which may characterize pyonephrosis in childhood.

(1) Male aged five years had been losing weight and energy for three months, eating poorly and crying a good deal. Micturition was painful and profuse, sweating especially at night had been noted. There appeared to have been no particularly acute onset. Latterly the boy had complained of pain in the right side, particularly in walking.

On admission, he was pale, lethargic and obviously ill. The temperature rose in the evening to 100° F. A large tender mass occupied the right renal area. The urine was turbid, sp. gr. 1030, alkaline, contained a trace of albumin and a fair number of pus cells. The cultures grew *B. proteus.*

The blood urea was 35 mgm. per cent.
Blood count R.B.C. 2,800,000 per c.mm.
W.B.C. 10,000 (75 per cent. polymorph.).
Hb. 48 per cent.
Following blood transfusion, the blood picture improved.
R.B.C. 4,375,000 per c.mm.
W.B.C. 18,000 per c.mm.
Hb. 65 per cent. C.I. 0·8.

The right kidney was urologically silent. The left appeared normal. A large lobulated pyonephrosis was removed, and the boy made an uninterrupted

FIG. 564.—"EMPYEMA" OF LEFT KIDNEY.

Excretion pyelogram of boy aged seven years, showing silent left kidney (normal right). Note the ringed shadows which were due to inspissated pus clots with phosphatic deposits.

recovery. Two months later his condition was excellent and the urine was clear and sterile.

(2) Male aged seven years, came to the out-patient department with a history of vague ill-health for two to three months, becoming gradually worse. No particular urinary symptoms had been noticed. On examination, the boy was pale and obviously ill. A large mass could be felt in the left loin.

Following admission, the temperature was found to be swinging (98° F. to 101° F.). The urine contained pus cells, and was heavily infected with *B. coli* and staphylococci. Blood urea was 44 mgm. per cent.; Hb. 68 per cent. Excretion pyelography showed the right kidney normal and the left "silent" (fig. 564).

The boy was given a small blood transfusion and twenty-four hours later the left loin was explored. An empyema of the kidney was revealed and a pint or more of stale greenish pus containing many soft phosphatic concretions

was evacuated, and the sac drained. The boy's condition speedily improved and the urine cleared.

One month later, after a further blood transfusion (300 c.cm.), an intracapsular nephrectomy was performed. Recovery was uneventful, and, when seen two months later, the boy was in excellent health.

PERINEPHRITIC ABSCESS occurs in childhood and presents the same problems of ætiology and diagnosis as in adults. Associated urinary manifestations—pus, bacteria or blood—may or may not be present. The prognosis is serious, and early diagnosis and effective drainage of the abscess must be the aim. "A third of all children with perinephritic abscess will die" (Campbell).

Male, aged ten years eleven months was seized with severe pain in the left loin with fever and occasional vomiting. The urine was said to have been dark in colour. After ten days' illness, he was brought to hospital. No history of injury or any other ailment could be elicited. On admission, the boy's temperature was 102° F., and he complained of great pain in the left side. There was fullness and loss of the natural curve in the left loin, with marked local tenderness and rigidity. No definite lump could be felt. The urine contained a few red cells but was otherwise normal and cultures proved sterile. X-ray examination revealed no bony abnormality, but pyelography was not done. The white cells totalled 16,900 per c.mm.

Four days later, the fullness in the left loin had increased, and the temperature was still oscillating. The white cells had now risen to 19,550 per c.mm.

The left loin was explored and a quantity of thick yellow pus evacuated from the perirenal area (*Staph. aureus*). The boy made an uninterrupted recovery.

Chronic infection of the urinary tract.—The majority of acute infections of the urinary tract clear up immediately in two to three weeks, if adequately treated along the lines indicated (p. 1540). Various extraneous factors, such as defective diet, general ill-health, particularly in relation to naso-pharyngeal infections, and gastro-intestinal disturbances may lower resistance and retard cure. Vulvo-vaginitis calls for special mention as a concomitant of obstinate infective cystitis in girls. The frequency with which the urinary infection disappears following effective treatment of the vulval lesion is clear evidence of a causal relationship.

In persistent or recurrent infections, particular attention must be paid to these possibilities. In the main, however, the causal factor in chronicity is to be found most often in the urinary tract itself. Whenever the symptoms, and especially the pyuria, persist with positive cultures after four to six weeks, and whenever bouts of infection recur, it should be the rule to instigate a complete urological investigation.

The root of the trouble is almost invariably obstructive, resulting in imperfect drainage of the urinary channels. In some children gross developmental defects will be revealed, which necessitate surgical intervention, perhaps of the most radical nature. In the lower urinary tract, meatal narrowing, stricture of the penile urethra, posterior urethral obstruction from valves, enlargement of the verumontanum, neuromuscular imbalance or sclerosis of the bladder neck and, at a higher level, lesions of the ureter or pelvis may be discovered. Happily, however, in many, no such abnormalities are found, and a reassuring prognosis can then be given.

It may well be asked why some children with a radiographically normal urinary tract should prove so resistant to treatment. But if the calibre and physiology of the child's passages, notably the ureter, is remembered, it will be realized that the œdema and reflex disturbances of peristalsis resulting in spasm, which accompany these inflammatory lesions, must very readily upset free drainage and so promote persistence of the infection. The passage of instruments, and the flooding of renal pelvis and ureters

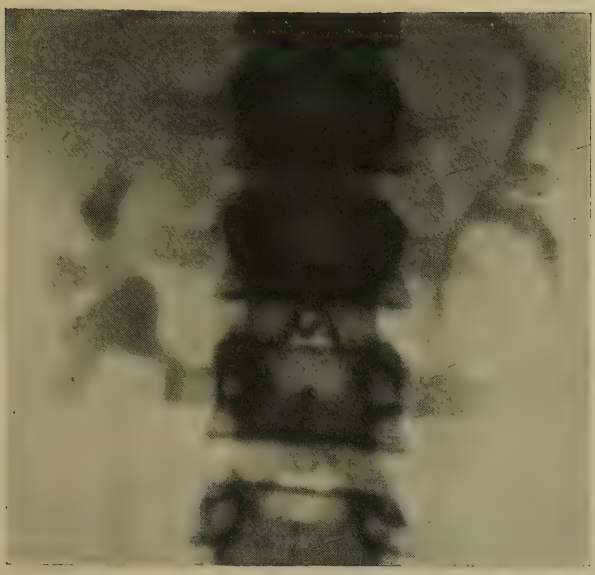
FIG. 565.—CHANGES DUE TO URINARY INFECTION.

Girl aged one year and five months. History of recurrent attacks of "pyelitis" from five months. Pyelogram (retrograde) shows clubbing of lower calyces of left kidney, probably resulting from chronic inflammation and spasm. Urine became sterile following instrumentation and course of potassium citrate and hyoscyamus.

involved in cystoscopy and pyelography, serves a useful purpose therapeutically, as well as diagnostically, in dilating and promoting drainage. Prompt disappearance of the infection is certainly a common sequel.

A close watch should be kept on all cases to ensure that the cure is permanent. Periodical catheter specimens are examined, and any persistence of symptoms or infection is an indication to repeat the instrumentation. Dilatation is in fact the sheet anchor of treatment.

It is important to realize that undue persistence of a urinary infection



A

B

FIG. 566.—PYELOGRAMS (EXCRETION AND RETROGRADE) SHOWING CHRONIC PYELONEPHRITIS OF THE LEFT KIDNEY WITH CONTRACTURE.

Note the shrunken calyces and narrow pelvis. The patient, a girl aged nine years, had suffered from enuresis and chronic urinary infection (*B. coli*) with acute febrile exacerbations for four years. Blood urea 26 mgm. per cent. Urine sterilized by sulphonamide therapy and enuresis cured.

inevitably leads to degenerative changes in the walls of the ureter and pelvis, to say nothing of the kidney itself (fig. 565, 566). Chronic dilatation (ureterectasis) or pyelo-nephritis thus determined, constitutes a serious outcome (see also under " Ureter ").

HÆMATURIA

Hæmaturia due to constitutional diseases, such as nephritis, scurvy, hæmophilia, or purpura calls for no comment here. The variety associated with some distant streptococcal focus, commonly in the naso-pharynx, is of considerable interest to the pædiatric surgeon. The writer has known a number of instances, in which the same organism, commonly a hæmolytic streptococcus, has been identified in throat or mastoid, and urine. The hæmaturia is usually brisk and painless, the general disturbance mild, and the course brief, the urine clearing in a day or two. Casts are virtually absent, and the condition disappears without sequel, though in a few cases, recovery is less rapid, and some blood may remain in the urine for a few weeks and some degree of permanent renal damage may ensue.

All other varieties of hæmaturia require urological investigation. The commonest variety is undoubtedly associated with meatal ulcer. The painful symptoms, the drop or two of bright blood usually at the end of micturition, and the obvious lesion make recognition simple, and no intricate investigation is needed. Acute infections—cystitis, pyelo-nephritis—may cause transient hæmaturia, especially in their early stages, as may some of the drugs administered for their relief. In such circumstances instrumental interference should be postponed.

In general, however, the passage of blood in the urine demands prompt elucidation, since it is likely to indicate a serious uropathy. It is a frequent early sign of urinary tract tuberculosis or calculus. It is not infrequent in renal growths, and it may occur in hydronephrosis, or congenital cystic kidney. In very rare cases, usually girls, renal bleeding occurs spasmodically, without any detectable cause, or particular bodily disturbance. The bleeding comes from both kidneys, though at the time of cystoscopy this may not be apparent. Hæmaturia of this type may come and go for a considerable period without any apparent interference with the child's health, and the precise nature of this so-called " essential hæmaturia " remains a mystery. Nævus of the renal papillæ has been described. In such a case the bleeding is unilateral and the only possible diagnostic sign is a filling deformity in the pyelogram.

Finally, in all instrumentation in childhood the utmost gentleness is essential if transient bleeding is to be avoided.

URINARY CALCULUS

Urinary calculi large enough to cause symptoms are rare in infants, but not uncommon in older children. Many factors may contribute to the formation of calculi in the urinary tract, *e.g.* undue concentration of the urine, stagnation resulting from obstruction or prolonged decubitus, infection (fig. 567 and 568), dietetic deficiencies or aberrations of

metabolism. The biochemical factors in stone formation are discussed by Higgins, Williams and Nash (1951).

Generally speaking, the most constant factor is urinary stasis, resulting from congenital developmental abnormality or acquired obstruction — together with the infection which is so commonly associated. In practice therefore, treatment, if it is to be effective, must remove the obstruction as well as the stone.

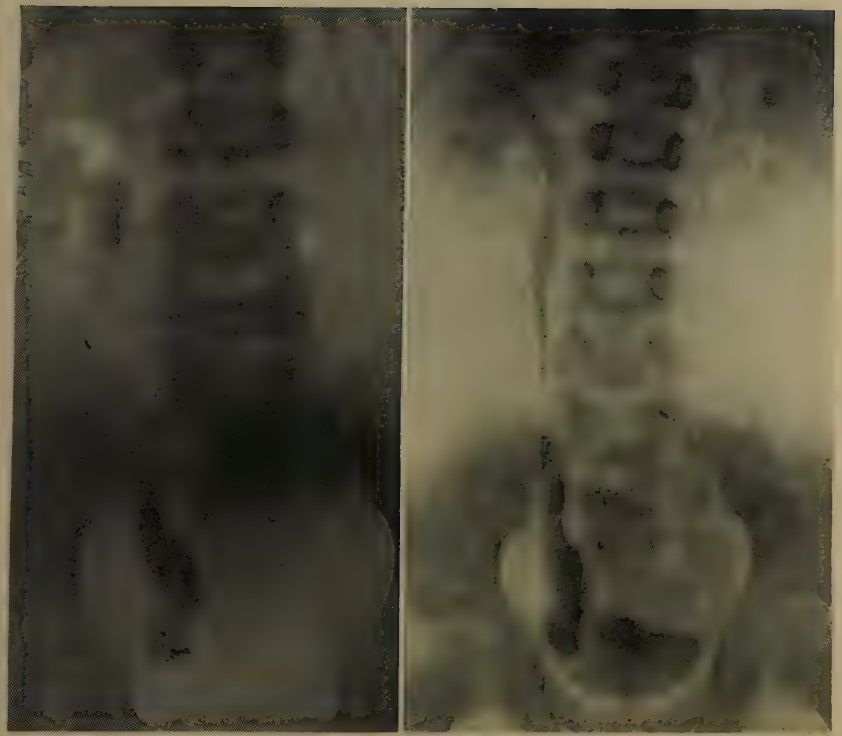
The prevalence of stone varies greatly in different countries. It is rare in England and Scandinavia, but common in Italy and Hungary, where Bokay has collected more than a thousand cases in children. In Eastern Russia stone is frequent, while in parts of India and Southern China it is extremely common. Thomas and Tanner in America found that the average age of the affected children was seven years, and the youngest ten months, in a series of 203 cases. It was roughly three times more common in boys than in girls. The stones were more often in the right kidney than the left, and in 69 per cent. of cases they had entered the bladder.

Fig. 567.—Retrograde Pyelogram. Girl aged seven. Stone in left renal pelvis.

Stone is more frequent among the poor than the rich, and especially among those who live on a poor diet principally of carbohydrates. Until sixty or seventy years ago it was common among children in England and Western Europe, but with the improvement in the standard of living that has taken place since then, it has become rare, while it is still just as frequent in Eastern Europe and Asia.

There is some experimental evidence to suggest that stone is a deficiency disease. Osborne and Mendel in America and McCarrison in India have produced calculi in rats, fed on a diet deficient in fat soluble vitamin. Noble, writing of vesical calculus in Siam, found the largest number of cases in the poorer agricultural districts; the greatest incidence being in the first ten years of life. "In Siam there can be no doubt that the children who suffer from stone have had a diet deficient in vitamin A."

Old statistics of bladder calculi show that they were more common in children than adults. In Sir Henry Thompson's series of 2,583 cases,



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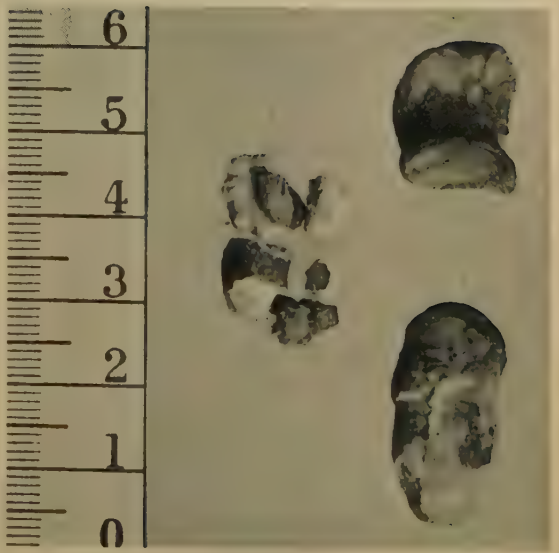

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E

FIG. 568.— URINARY CALCULUS.

Boy aged four. Pyuria two years (*B. proteus*).

(*A*) shows multiple calculi in right ureter. (*B*) Excretion pyelogram showing dilatation of right pelvis and ureter. At the first operation the stones were removed (*C*), composition mainly phosphatic. The ureteric orifice to the bladder was freely dilated. Following this operation the pyuria persisted. A further retrograde pyelogram nine months later (*D*) shows gross dilatation of the ureter and a further large calculus at the lower end. At the second operation nephro-ureterectomy was performed (specimen shown in *E*). Result: cure.

1,281 were in children under sixteen. Assendelft found 77 per cent. under ten in 630 cases, in Russian hospitals, and Freyer 274 out of 871 under ten in India. Stone in the bladder is much less frequent in this country than in former times, but there is no statistical evidence that this is true of renal calculi. Probably this discrepancy is accounted for by the fact that renal calculi are more readily recognized now than in the past.

Small uric acid deposits are found with some frequency at autopsy in the kidneys of infants. These are "primary" calculi, being pure crystalline precipitations from the urine. The passage of such crystals may cause urgent symptoms and hæmaturia. In older children transient attacks of this character are met with in the summer time from excess of fruit in the dietary. Abundance of oxalate or uric acid crystals in the urine affords confirmatory evidence of the cause.

The larger calculi are "secondary," being composite in structure, with a nucleus of inflammatory debris, blood clot, a primary crystal, or a foreign body. The commonest are mixed calcium oxalate and urates. Pure uric acid stones are rare. Sodium and ammonium urate form pale brown soft calculi. Phosphatic stones are usually rapidly formed, are light coloured and crumble easily.

Stones are frequently laminated, the common ones consisting of alternate layers of calcium oxalate and uric acid; if the urine is alkaline, a deposite of phosphates occurs on the surface. A special variety is the rare cystine calculus. Cystinuria results from an inherent defect in metabolism, described on p. 346. Crystallization with calculous deposition is prone to occur.

Density to X-rays.—This varies with the composition of the stone. The densest shadows are given by oxalate of lime and cystine, those from phosphatic calculi are poor. Pure uric acid stones are seldom demonstrable, except as filling defects.

Symptoms.—Renal calculi may exist for a considerable time without giving rise to symptoms. The common loin pain is less frequent in children, and the symptoms and signs are more often those of a chronic infective pyelitis, the stone being revealed in the course of investigation for infective pyuria, with or without hæmaturia. Hæmaturia alone may be the initial sign.

If the stone works loose and engages in the renal pelvis or ureter, classical colic results. "Nine out of ten stones engaged in the ureter will spontaneously pass to the bladder" (Meredith Campbell). If retained in the ureter, the stone commonly lodges at the lower end, and a stricture will usually be found to be the determining cause of such lodgement. Dilatation of the ureter follows and the stone may then slip up and down the enlarged ureter (fig. 568), a fact which sometimes complicates operative removal. Small stones, on the other hand, may become so tightly incorporated with the ureteric wall as to make removal difficult on this account.

Stones in the bladder may occasionally form primarily around a foreign body, but almost all are of renal origin, though their passage through the ureter may not have been marked by any definite history of colic. The

bladder stone gives rise to painful and frequent micturition and sudden stoppage of the urinary flow may provide a suggestive sign. Impaction in the urethra happens occasionally. It is said to be especially liable to occur in boys about the age of two, causing severe local pain and distension of the bladder. Small calculi may be passed.

Diagnosis.—An attack of spasmodic abdominal pain, dysuria, vomiting, without diarrhœa and with rapid recovery is a characteristic clinical picture of renal colic, and should lead to an examination of the urine for blood and pus cells. But in infants too young to describe the locality of the pain, diagnosis is more difficult. Radiography should be used in all suspected cases, but it must be remembered that stones may be big enough to give violent colic, but too small to throw a recognizable shadow, so that a negative result by this method of examination does not exclude the diagnosis of stone.

Cystoscopy should always be done in the case of a renal or ureteric stone. The presence of the other kidney must be confirmed, and if there is any question of nephrectomy its functional value must be estimated.

Treatment.—The treatment of calculi in children is the same as in adults. In all cases the question of removal of the stones by operation has to be considered, and when there are clear indications for it, this should not be delayed. The danger of delay is that a calculous pyelitis, or pyonephrosis, may arise; and if the sepsis is bilateral, irreparable damage will be done unless operation is carried out. For the colic, warmth, alkaline diluents and narcotics are required, and during the intervals, the patient should drink water freely.

In the case of an impacted ureteric calculus, the passage of a ureteric catheter up to the stone, and the introduction of procaine 2 per cent. followed by 2 c.cm. of liquid paraffin is well worth a trial.

Stone in the bladder in small children is best treated by a supra-pubic cystotomy. The operation is simple and the bladder should be closed unless cystitis is present, when a tube should be left in for a few days. If the bladder is closed a temporary drain should always be placed in the space of Retzius.

REFERENCE

Higgins, T. T., Williams, D. I., and Nash, F. E. (1951). *The Urology of Childhood*, London, 164.

NOTE ON THE SURGICAL ASPECTS OF ENURESIS

Disturbances of the normal neuro-muscular mechanism feature prominently in many of the urological disorders already described. Frequency, urgency, wetting are distinctive symptoms, whilst spasm and peristaltic irregularities up and down the urinary tubes constitute a factor of first rate importance in determining persistence of infection, pain of urogenic nature and even of acquired gross anatomical distortion. The term "*enuresis*" should therefore be used with circumspection and due appreciation of the latent possibilities.

The normal infant, sensibly attended, may be expected to acquire reasonable bladder control by the end of the first year or soon after. It may be earlier in some and later in others, environment, training and individual health and temperament differ. After the age of two years, however, " accidents " should be rare. After three-and-a-half to four years they should be virtually unknown. Persistent wetting between two and four in an otherwise healthy infant should arouse disquietude. Some serious abnormality of the urinary tract is a possibility. Confirmatory evidence may be afforded by bouts of fever and the passage of " milky," purulent or evil-smelling urine.

Only after the age of four years should persistent lack of control be designated " *enuresis.*"

This disorder has been well defined as " The involuntary and usually unconscious voiding of large amounts of urine, which occurs predominantly during sleep, in the absence of organic disease of the nervous or urological systems " (Zappert quoted by Meredith Campbell).

In the main, this is a functional disturbance without any organic basis and should be treated as such (see p. 1120).

But the proportion of children in whom an organic disorder is, in fact, present, is much higher than is often supposed—*approximately 1 in 10*—and it is obviously important to sort out this group.

Many of the uropathies can be recognized without much difficulty at the outset by adequate clinical examination. Careful inquiry into the history may be suggestive, *e.g.* frequent and urgent voiding of small quantities of urine, pain and febrile attacks, suggest a urinary infection. Straining and difficulty in the act of micturition point to a possible urethral obstruction. Particular examination should be made of the external genitals—in the girl, vulvo-vaginitis and urethral abnormalities —in the boy a contracted or ulcerated external urinary meatus may be found. " Phimosis " has no bearing on enuresis and, in the writer's view, circumcision has no place in the treatment. The bladder may be found distended, and the presence of residual urine in appreciable quantity points to a probable obstructive lesion. A complete urinalysis should always be done, including culture to exclude infection.

As regards organic disorders of *the nervous system*, apart from gross mental defects, there is the vexed question of spina bifida. Spinal fusion errors are demonstrable radiologically in many children. Authorities vary from 15 per cent. to as high as 35 per cent. But it is certain that spina bifida is a very rare cause of enuresis. Sacral defects which involve the parasympathetic fibres (S2, 3 and 4) to the bladder can undoubtedly cause disturbances of control. Accompanying neurological signs— " saddle " anæsthesia, etc.—are almost certain to be present.

There is little evidence that defects at a higher level involving the sympathetic roots (L1 and L2) may cause enuresis.

Assuming that the preliminary examination of the child has failed to indicate any obvious organic explanation for the enuresis, the usual medical treatment is instituted. Nevertheless, if after three months no satisfactory improvement has followed, the urological surgeon should be

consulted. It will be found that a high proportion of these failures have an organic basis for their disability.

TUMOURS OF THE KIDNEY

Benign tumours of the kidney, fibroma, adenoma, lipoma, lymphangioma are unusual and of little clinical importance. The very rare nævoid

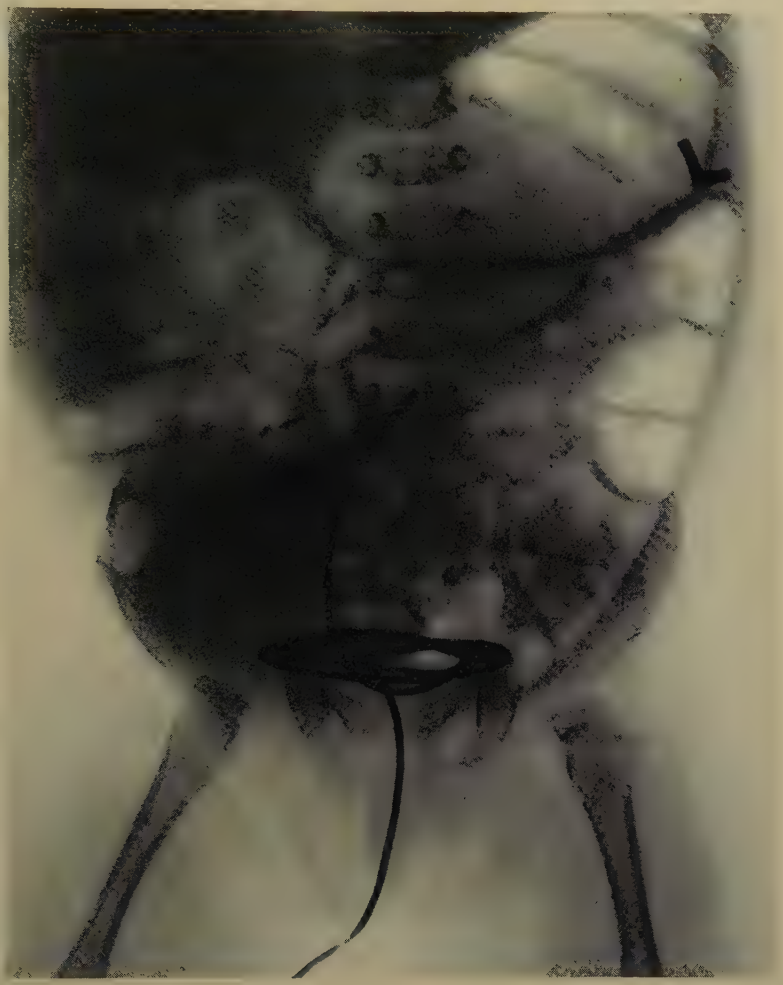


FIG. 569.—LARGE TERATOMA OF RIGHT SIDE OF ABDOMEN EXTENDING ACROSS MIDDLE LINE, SHOWING OSSEOUS DEPOSITS IN CHILD AGED EIGHT WEEKS. PYELOGRAM OF DISPLACED RIGHT KIDNEY.

Removal of teratoma, recovery.

growth may cause puzzling and troublesome hæmaturia. Swan and Balme (1935) reported a case, occurring in a boy of fifteen years, and analysed twenty-six others previously reported, all in adults.

The kidney is, however, a frequent site of malignant growths in childhood and the tumours of this nature, which may be met with in the renal area, are of great interest and importance.

1. Pararenal tumours.—The *teratoma* illustrated (fig. 569) was successfully removed by Addison and the writer, and the child remained well ten years later. Meredith Campbell (1937) describes a similar case, successfully operated on by him, and refers to four others.

2. Tumours of the suprarenal.—(*a*) CORTICAL.—Adenomas or

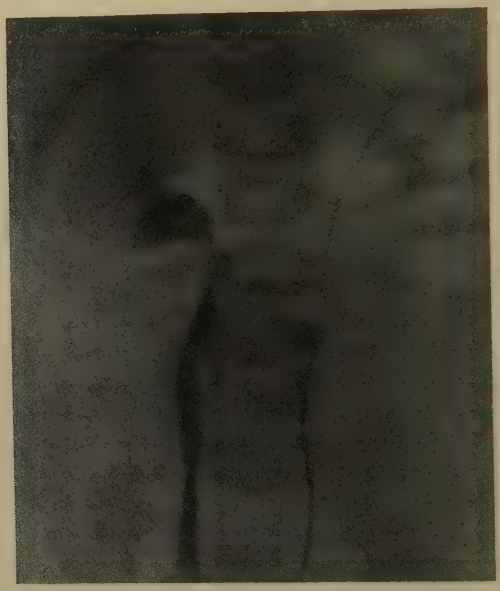


FIG. 570.—RETROGRADE PYELOGRAM SHOWING DISPLACEMENT DOWNWARDS OF RIGHT KIDNEY BY A TUMOUR OF THE ADRENAL.

This girl, aged one year and four months, had marked hirsute precocity with bodily overgrowth. An adrenal tumour was suspected. The pyelogram confirmed the diagnosis and location. A right adrenal tumour (size 3 × 2 × 2 cm.) was removed (pathology—carcinoma). Seven years later the child remains well and is now normal in every way.

carcinomas may form pararenal tumours of some size. They are characterized by profound anomalies of sexual development, virilism, precocious puberty and so on, which serve to distinguish them from renal growths. Pyelography demonstrates displacement, rather than distortion of the renal pelvis, which may be helpful in distinguishing them from Wilms' tumours. Pyelography may also serve to indicate the side affected, when such growths are too small to be palpated (fig. 570).

(*b*) MEDULLARY.—NEURO-BLASTOMA OR "SYMPATHO-BLASTOMA". These tumours, which may originate either in the medulla of the suprarenal or in other sympathetic elements, produce large retroperitoneal

growths in the pararenal area. They are highly malignant, and disseminate in the liver (Pepper type) or the bones, particularly the long bones and skull (Hutchison type). Stern and Newns (1937) emphasized the importance of initial pains in the legs and limping, due to periosteal involvement, in addition to the abdominal swelling. Periodic fever and characteristic blood changes (hypochromic anæmia) are also common features. Differential diagnosis from Wilms' tumour may not be easy. Pyelography, in addition to the clinical features enumerated, may help; the renal pelvis tends to be less distorted than in renal growths.

(*c*) Retroperitoneal sarcoma occurs much less frequently than the neuro-blastoma or Wilms' tumour. It is usually more medial in position and fixed to the spine.

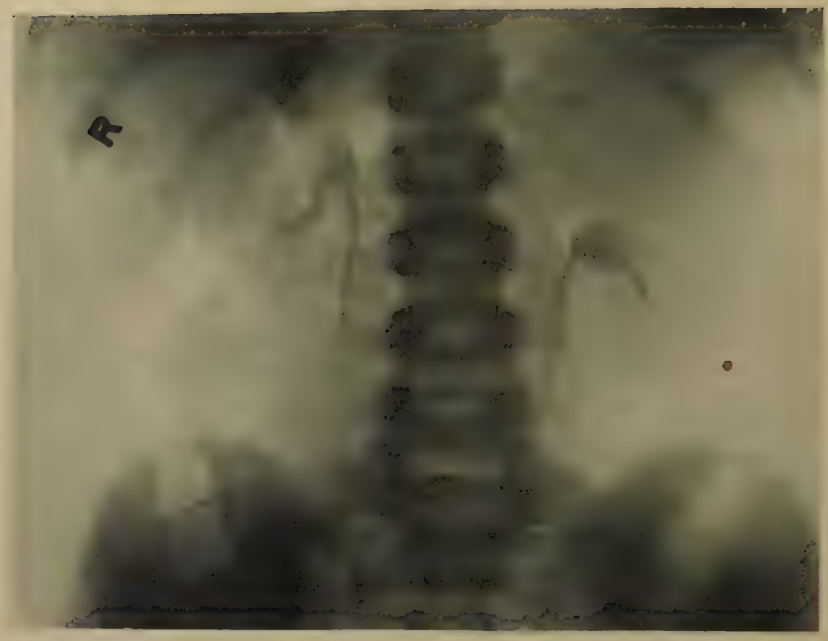
Wilms' embryoma.—The highly malignant Wilms' tumour (embryoma, adeno-sarcoma, nephro-blastoma) is one of the commonest growths met with in childhood. Its incidence about equals that of the neuro-blastoma. The origin of these growths is still undecided, whether from undifferentiated cells of the Wolffian ridge, which become isolated as potential tumour masses (Wilms), or from the metanephros (Busse and Nicholson), but their histology is well known. Sections display a conglomeration of spindle, oval and round cells, either entirely undifferentiated or in varying degrees of differentiation into disorderly masses which may show primitive tubules of varying types and shapes, hyaline masses and often striped muscle fibres and cartilage nodes. The growths are excessively vascular and destructive hæmorrhages and areas of necrotic softening are frequent. Wide variations are seen between individual tumours and between different areas of the same tumour.

The tumour grows rapidly, invading the adjacent lymph glands and very frequently the blood-stream, producing metastases most commonly in the lungs. The growth may extend directly into the ureter, the vena cava, the diaphragm or the peritoneum, possibly leading to intraperitoneal bleeding as in a case recorded by Tanner (1943). Characteristically the tumour, while entirely involving the kidney, usually remains partially encapsulated and distinct from the gland, pressing upon and often flattening it out to a thin strip at the periphery. This explains the distortion of the renal pelvis which is such a distinctive feature in the pyelograms.

Occasionally an "extrarenal" type is seen in which the kidney suffers less direct compression.

Clinical features.—Wilms' tumour is a growth of early life, almost all instances occurring in the first five years, the majority in the first three. The onset is insidious, and enlargement of the belly is commonly the first sign, which unfortunately means that the tumour is already of considerable size. Hæmaturia is uncommon. (In one case of the writer's, a baby of ten months, it was the presenting sign, but examination revealed a large tumour previously unsuspected, in the left renal area, and any manipulation of this produced a brisk hæmaturia.)

There is nothing characteristic in the blood picture, which usually



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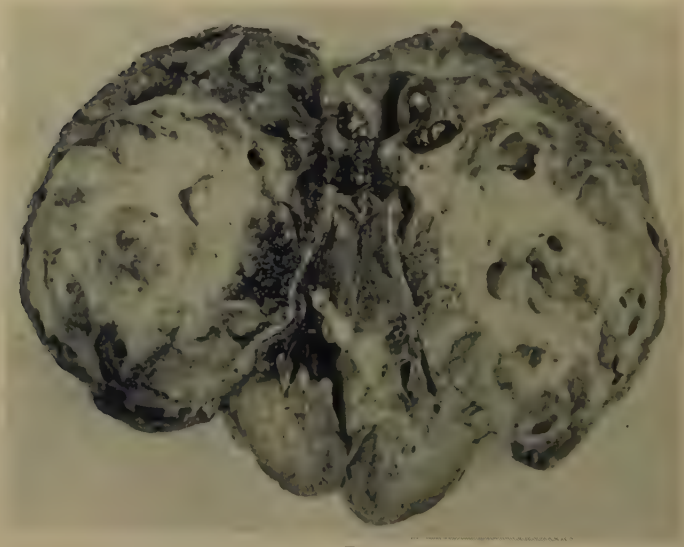

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FIG. 571.—WILMS' TUMOUR. UPPER POLE OF LEFT KIDNEY SIMULATING AN ENLARGED SPLEEN.

Girl aged four years. (*A*) Pyelogram shows depression of the pelvis and distortion of the upper pole. Pre- and post-operative radio-therapy. Death nine months after operation. (*B*) shows growth.

shows a secondary anæmia of greater or less degree. Pyrexia is unusual, though it may occur. The pyelogram is characteristic. The excretion method is best, when possible. The pelvis is grossly distorted; often only a fragmentary shadow may be visible and sometimes none at all.

Diagnosis.—The following may simulate a Wilms' tumour:

(1) A tense cyst, *e.g.* hydronephrosis, congenital cystic kidney, or other renal or pararenal cyst. Transillumination is often useful and pyelography is usually confirmatory.

(2) Neuro-blastoma. The lump usually appears higher and more median in the abdomen, more deeply seated and more fixed. The distinctive clinical features, bone pains, fever, and blood picture may give the necessary clue. Metastases in bone are not a feature of Wilms' tumours. The pyelogram tends to show displacement rather than distortion.

(3) Splenic enlargement may sometimes cause doubt on palpation alone, and a Wilms' tumour arising in the upper renal area may simulate an enlarged spleen (fig. 571) (see also fig. 572 and 573). Pyelography is diagnostic. The kidney may, though rarely, be depressed by an enlarged spleen but the pyelogram shows no distortion.

(4) Retroperitoneal sarcoma is usually in the mid-abdominal rather than the renal area, and tends to be more fixed to the back wall of the abdomen.

Treatment.—The results of the treatment of Wilms' tumour, whether by operation or radio-therapy, or a combination of the two, are so universally disappointing that it may well be asked whether one should attempt it at all. The answer is that an occasional child's life is saved, which justifies the effort and encourages the hope of better results in the future. It is unfortunate that the growth is usually well advanced before a diagnosis is possible. Many cases are inoperable when first seen, either by reason of their size, or the presence of demonstrable metastases. A preliminary radiogram of the chest should always be taken. If secondary deposits are visible in the lungs, the case is beyond surgical aid. The removal of tumours, which extend far across the middle line, should not be attempted unless reduction to operable proportions can be first achieved by radio-therapy. Those tumours in which undifferentiated calls predominate shrink dramatically. On the other hand those with more extensive differentiation tend to respond very little. Tumours, which are of operable size, and without demonstrable metastases, should be removed. The question of pre-operative irradiation has to be considered. The writer's present opinion favours immediate operation. Delay and repeated palpation of these tumours greatly increase the risk of metastasis and there is, as yet, no evidence that pre-operative irradiation offsets this risk. If there is any appreciable degree of anæmia, a small pre-operative blood-transfusion should be given. The most satisfactory anæsthetic is intratracheal gas—oxygen—ether. Then with due care, gentleness and meticulous hæmostasis, there need be little anxiety as to the operative risk.

The tumour may be approached (1) by the retroperitoneal route from

the loin or (2) transperitoneally through a paramedian incision. The latter in theory offers the advantage of ligating the pedicle vessels first but the tumour mass seems very often to make this difficult. In some cases the writer prefers the lateral route. The essential point is that the incision should be of adequate size. It is made transversely and extends from the mid-line in front to the spine behind. The rectus is divided if necessary. The peritoneum is freely open in most cases and any portion involved by the tumour is removed. Peritoneal repair always seems more easily accomplished than in the anterior approach. The tumour is handled with gentleness, and removal is as

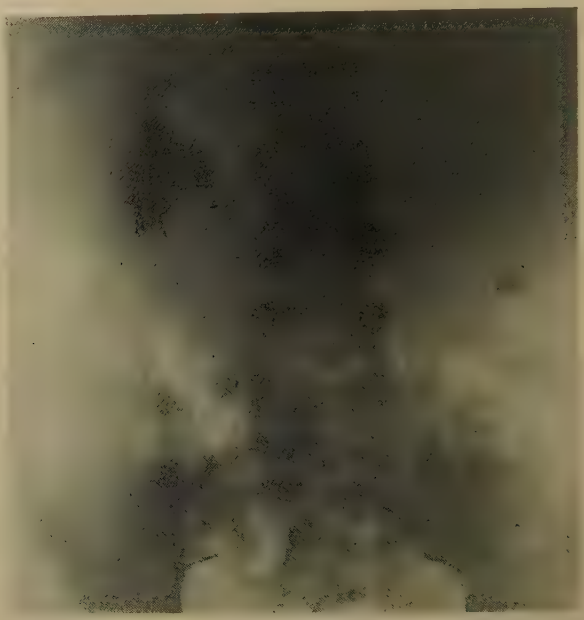

FIG. 572.—WILMS' TUMOUR IN BOY AGED SEVEN YEARS.

Excretion pyelogram showing displacement and deformity of left renal pelvis. Tumour removed. Nine months later death with lung metastases.

comprehensive as possible—to include all perirenal fat, the suprarenal, all lymph glands in the vena caval area, and as much of the ureter as possible. The wound is closed by accurate suturing of muscles, layer by layer, and a small drain is employed for thirty-six to forty-eight hours. Recovery is straightforward, and operative deaths should be rare.

Post-operative irradiation, if it is to be employed, should begin as soon as the wound is healed. Its value cannot yet be assessed. Unfortunately the end results, with or without it, remain bad. Recurrence of the growth either locally or metastatically is the rule often within six months. But it must be repeated that there are exceptions.

The rare fibro-cystic papilliferous type of growth, of which the writer

has seen a few cases, is of a much more hopeful nature, and cannot be distinguished until excised.

FIG. 573.—PYELOGRAM SHOWING DISPLACEMENT OF URETER AND EARLY HYDRONEPHROSIS RESULTING FROM A COLUMNAR-CELLED-PAPILLOMATOUS CARCINOMA OF RENAL PELVIS.

Child aged one year eight months.

Occasionally on histological evidence, a tumour turns out to be carcinomatous arising apparently in the epithelium of the renal pelvis. It cannot be said, however, that this alters the prognosis (fig. 573).

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TUBERCULOUS INFECTION OF THE URINARY TRACT

Introductory.—Apart from the terminal stages of a generalized miliary infection, tuberculosis of the urinary tract has been regarded as a rare disease in children, and as one having a high mortality rate. It is probable that the closer and more accurate observation made possible by modern methods as well as modern drug therapy (streptomycin) will modify this view. Already it may be surmised with some confidence that involvement of the urinary organs is not uncommon in tuberculosis of childhood and that, despite the undoubted gravity of such a complication, the prognosis may be less gloomy than has been supposed.

Pathology.—The disease is almost invariably blood-borne and the primary lesion is renal. Initial ascending infection must be rare. Meredith Campbell quotes Wildbolz (1908–9) as demonstrating that infection by this route could only be produced experimentally in the presence of previous obstruction or inflammatory injury to the uretero-vesical mechanism.

This section is not concerned with the overwhelming invasion of both kidneys seen in the terminal stage of acute miliary tuberculosis, but only with the more chronic instances where the balance between the contending forces of infection and resistance is more favourable to the patient. As this balance may happen to be poised, so will vary the resultant pathological changes and the patient's prospects of recovery.

A hæmatogenous infection implies the existence of a primary focus elsewhere. This may be an old inactive lesion, discoverable with difficulty or not at all. On the other hand it may be concurrently active. It is coming to be recognized that, in the presence, *e.g.* of active bone tuberculosis, renal infection is not uncommon. Addison emphasized this and stated that " in the early stages, which may persist for some years, there are no urinary symptoms whatever, and the pyuria is so slight, and often so intermittent, that it escapes notice unless very careful and repeated microscopical examinations of the urine are made."

Small foci of disease in the kidney, as elsewhere, may undoubtedly undergo resolution, with curative fibrosis. This must explain the instances of transient and non-recurring tuberculous bacilluria. The writer has watched two such cases over six and eight years respectively, both children remaining perfectly well. The observations of Helmholz (1934), Medlar (1926) and Band (1935) afford proof that mere filtration of tubercle bacilli through the kidney does not occur, but that microscopical renal lesions are invariably present, when bacilli are passed in the urine.

Once a sizable focus has developed, usually in the cortex, it tends to spread to the pyramids, with the usual combination of caseation and

fibrosis. Progress is often slow and intermittent, and in favourable circumstances may be arrested. At first it is usual for the disease to be confined to one side, an important fact, since early eradication of the involved kidney may ensure a cure. Ultimately the pelvis and ureter are infected, the ureter becoming thickened and the lumen narrowed. Constriction of the pelvi-ureteric junction may lead to a hydronephrosis, which usually precipitates a rapid exacerbation of the destructive process in the kidney. Thickening and fibrosis of the ureter lead to shortening and the well-known deformity of the vesical orifice (" golf-hole ureter "). Extension to the bladder follows, causing a patchy cystitis, first manifested around the ureteric orifice of the affected side—later becoming more widespread and eventually ulcerative. Involvement of the bladder materially aggravates the symptoms ; sooner or later the cystitis affects the ureteric opening of the sound side, leading to defective functioning of the uretero-vesical valve mechanism, which is the prelude to involvement of the opposite kidney by ascending infection.

" Tuberculo-toxic nephritis."—Meredith Campbell emphasizes the common association of this condition—an irritative nephritis of the " sound " renal tissue from circulating tuberculo-toxin originating in the active foci. The urine contains albumin, many casts (epithelial, hyaline and granular) and sometimes red blood cells. The nephritic outbreak may be quite temporary, but, if of longer duration, constitutes a bad prognostic feature.

Symptomatology and clinical signs.—The outstanding feature is the insidious nature of the early stages of the disease. It is probable that not a few children achieve a natural cure, without the renal involvement ever being recognized. It is certain that, in most cases, the disease has progressed considerably before a correct diagnosis is made.

Addison has given an admirable description of the symptomatology and diagnosis, which cannot be improved upon and merits quoting in full :

" In the earliest stages of invasion of the kidney there are no symptoms, and the only sign is a very slight pyuria, usually intermittent, and discoverable only on microscopical examination. The tubercle bacillus can be found by the inoculation of guinea-pigs with a considerable quantity of centrifugalized urine.

Hæmaturia is almost invariably the first objective sign, seldom more than slight in amount, and frequently present only for twelve or twenty-four hours. The hæmorrhage subsequently recurs at intervals associated with an increasing pyuria, and in the later stages of general bladder involvement is usually a constant feature.

The urine is acid, and until the disease is well advanced is seldom contaminated with other organisms. In the later stages *B. coli* and streptococci are usually found. The general health is unaffected at first, and it is not until the urinary symptoms, pyuria, and increased frequency become marked that some loss of weight and general failure of health become evident. A little irregular pyrexia, the temperature rising to 100° F., is often present in the more active stages, but frequently the temperature remains normal for considerable periods. In the later stages, where the kidney is disorganized, an irregular temperature, reaching 102° F. at night, is usual. A sudden

febrile attack with a temperature of 103° F. or more, is not unusual where there is *B. coli* infection. Pain is never a marked feature in an uncomplicated case, though some aching may be present if the disease is very active. Where there is a *B. coli* infection with acute febrile attacks severe renal pain is usual during the attacks. The pain may be referred to the abdomen. On examination the kidney is usually not enlarged, but when practically completely disorganized may be moderately increased in size and become a little tender.

Increased frequency of micturition, difficult to be certain about in a child until it becomes very marked, does not occur until the bladder is involved. When the bladder is infected increased frequency of micturition is always present, at first more noticeable during the day. As the bladder becomes more inflamed and ulcerated the frequency increases until complete incontinence is established.

The most striking feature of the whole clinical picture is the complete absence of pain on micturition, either during or at the end of the act, even when, as frequently happens, the bladder capacity is reduced to an ounce or less. If pain does occur in an occasional instance it is due to an active *B. coli* or streptococcal infection.

Diagnosis.—The diagnosis is made on the discovery of the tubercle bacillus, and in every case of unexplained chronic or intermittent pyuria a careful search must be made. The bacillus is difficult to find in an early case, and often is only intermittently present. Examination on several occasions may be necessary before the search is successful. A twenty-four-hour specimen of urine should be collected, and centrifugalized for microscopical examination, and if this fails to show the bacillus the residue must be injected into a guinea-pig before tubercle can be excluded.

Even in an advanced stage of the disease the signs and symptoms are merely those of chronic cystitis—that is, pyuria, and increased frequency or enuresis. X-ray examination may show increased density of the kidney, or even calcareous areas, when disorganization has occurred, and an intravenous pyelogram will show irregularity of the pelvis and destruction of calices. Owing to the difficulty of getting a good picture by the intravenous method it may be worth while to use the ureteric method in certain cases where it is desirable to find out how much the kidney is affected. The ureteric method has been condemned as being apt to spread the disease further, but I do not think this is a really serious danger, except in an early case. Cystoscopy is always necessary.

At first the bladder may appear perfectly healthy, or a little redness and swelling may be seen round one ureter. Later a few tubercles and one or two small ulcers appear round the affected ureter, followed by inflammation of the trigone and the further spread of tubercles and ulceration on the base of the bladder. Ultimately the inflammation becomes general, and œdema and ulceration increase to such an extent that it is often impossible to find the ureteric orifices."

Prognosis.—This must vary with the circumstances of the individual case. Unfavourable points are:

(1) The existence of an active lesion elsewhere, *e.g.* bone, joint, lung.

(2) The persistence of nephritic signs. Albumin, casts and blood cells in the urine with evidence of depleted renal function.

(3) Extensive disease—especially with involvement of the bladder or both kidneys.

But in an early localized case the outlook may be good and even in quite advanced cases the disease may still be arrested under favourable circumstances. As is well known, surgical extirpation of the main lesion when this is practicable may be curative.

Treatment.—The first requisite is rest, and sanatorium treatment along the well-known lines. The urologist's main function is to elucidate the precise nature and extent of the disease. If it can be clearly shown that the involvement is unilateral and that it is advancing, or is already sufficiently extensive—a nephro-ureterectomy becomes a clear surgical indication; the results are usually excellent. This holds good even when the bladder is involved.

When the second kidney is also affected, it may still be worth while to remove the worse kidney, though the decision calls for fine judgment, particularly if an active focus coexists elsewhere. Naturally the prospects in such a case are far less favourable.

The introduction of streptomycin has radically altered the outlook. A high concentration in the urine is easily obtained with relatively low dosage. For a child 0·1 to 0·2 gm. twice a day intramuscularly is about the range. Para-aminosalicylic acid should be given as well. The treatment may have to be continued for six months and can cure the condition completely without other active measures. The question of nephrectomy must be reviewed in the light of the progress made but it is likely that surgery will be required less and less. The value of other new drugs is less well defined. The thio-semicarbazones (Domagk *et al.*, 1950) for example, do not appear to be as effective as streptomycin.

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CHAPTER XXXIV

VENEREAL DISEASES

DAVID NABARRO AND MARY MICHAEL SHAW

SYPHILIS

Children of all ages are as liable to syphilis as adults, but owing to the fact that the contagion is usually passed from one individual to another during sexual intercourse, cases of acquired syphilis are naturally rarer in childhood, and when they do occur the primary lesion is usually extra-genital. Syphilis is unique among the infectious diseases in that it is transmissible to the offspring—not as an exceptional event, but as a practical certainty in the case of early disease in either parent. Frequently it is the father who is infected first, then the mother and finally the child who, according to most recent authorities, becomes infected by the trans-placental route. A considerable percentage of the mothers of syphilitic children give no history and show no signs of syphilis, yet most of them have a positive Wassermann reaction and must be regarded as having latent syphilis. This is doubtless the explanation of Colles's law, which states that the suckling of a syphilitic infant by its apparently healthy mother does not result in her infection, whereas if another—healthy—woman suckle the same child she may develop a chancre on her breast. There are, however, some probable exceptions to Colles's law, and the infectivity of congenital syphilis has certainly been exaggerated. The doctrine that the healthy children of syphilitic parents are immune from syphilis has been dignified with the name Profeta's law, and exceptions to it are said to occur not infrequently. Actually, all that Profeta stated was that "the healthy child of a syphilitic mother could be suckled by her, or by a syphilitic wet nurse, with impunity," and it is due to subsequent writers that this modest contribution of Profeta to clinical syphilology has been changed into something more comprehensive and, incidentally, incorrect.

Acquired syphilis in infants and children does not differ materially from the adult form in its pathology, course and symptoms. In congenital syphilis, on the other hand, the fœtus may possibly be infected at the time of impregnation of the ovum and develop hand in hand, so to speak, with the syphilitic virus, which usually leads to early death of the fœtus with abortion. Most authorities state that infection of the fœtus does not occur before the fourth or fifth month of pregnancy, for it is rarely possible to demonstrate the treponema in fœtal tissues before that period, but from the fifth month onwards the fœtal tissues often swarm with treponemata, since the fœtus offers practically no resistance to their multiplication. Even in the absence of infection of the fœtus itself, syphilitic disease of the placenta may lead to early abortion. Several authorities maintain,

however, that the role of syphilis as a cause of abortion and stillbirths has been overestimated, and it certainly appears to be the case at the present time that the classical syphilitic family history of several abortions or stillbirths, followed by premature births, and eventually the birth of a living but syphilitic child, is rarely obtained from mothers. In a considerable proportion of the cases which have attended the clinic at The Hospital for Sick Children, Great Ormond Street, the syphilitic child has been the mother's first offspring. This change from the sequence of events which formerly obtained may be due either to a natural modification in the severity of the infection in the parents, or to a diminution of virulence consequent upon the better treatment of the fathers since the introduction of the arseno-benzene compounds and the establishment of venereal diseases clinics (1917).

In addition to the early infection of the ovum referred to above, the fœtus may be infected later on in the pregnancy, possibly, as Rietschel (1927) suggests, by extension of the uterine disease to the placenta before birth, or at about the time of birth during the gradual separation of the placenta from the uterus. The maternal and fœtal bloods then mix and during the uterine contractions the spirochætes are carried in varying numbers into the fœtal circulation. This would explain the latent period of the disease which may be as long as twelve weeks.

The *viscera*, which are only affected in the late stages of the acquired disease, are in congenital syphilis often attacked early and severely, causing death either *in utero* or in the first few weeks of extra-uterine life. In these visceral lesions the treponemata can be found in enormous numbers, in contrast with their scarcity in the lesions of acquired syphilis. The liver, owing to its situation and great importance in the fœtal circulation, is the viscus most frequently affected, and a peculiar type of cirrhosis results, in which the new fibrous tissue besides being interlobular also invades the lobules and penetrates between the individual cells.

The *growing bones* are also often attacked, as was first pointed out by Wegner who published his classical description of the histo-pathological changes of syphilitic osteochrondritis in 1870. Parrot, who made extensive clinical and pathological studies of the bones in syphilitic fœtuses and infants, regarded the process as a syphilitic dystrophy, that is, a nutritional disturbance of the bone-tissue at the point of ossification, and disagreed with Wegner's conception of an inflammatory origin of the syphilitic process. He found that the bone lesions did not appear until the fifth month of intra-uterine life and he maintained that *all* syphilitic infants were affected and that *every* bone of the skeleton was involved.

In the main there is agreement among observers as to the macroscopic and, to a less extent, the microscopic changes seen in syphilitic bones, but some authorities such as Hochsinger, Turnbull and others agree with Wegner that the process is an inflammatory one, whereas Stafford McLean and others agree with Parrot that it is rather a process of disordered functional activity—" diminished osteoblastic action with lawlessness of

growth, excessive osteoclastic activity leading to resorption of varying parts of the metaphyses and diaphyses" (McLean, 1931).

FIG. 574.—SYPHILITIC OSTEOCHONDRITIS AND OSTEOMYELITIS FROM A CHILD AGED THREE MONTHS.

Note the resorption of various parts of the ends of the bones and of the shaft.

Macroscopically there is a yellow irregular line at the junction of the epiphysis and metaphysis, which is due to an increase in the depth of the zone of provisional calcification. This appearance is suggestive, though not conclusive, of syphilis, but when associated with rarefaction (softening) and loss of cortex at the upper and inner aspect of the tibiæ, it is pathognomonic of congenital syphilis. The deepened metaphyseal line is pink instead of being yellowish and feels gritty to the point of the knife, the grittiness being due to over-calcification, whereas the rarefied or softened parts of the bones appear to be almost devoid of lime salts and can be easily cut with a knife. Sometimes the deposition of lime salts in the cartilage occurs irregularly as projections, giving rise to a zigzag appearance of the metaphysis—the "saw-tooth edge." At other times the bones show a variable amount of submetaphyseal rarefaction, well seen in skiagrams—which may be due to the toxic action of the treponema or to the accompanying anæmia. Osteomyelitis and osteitis may also be found as is evidenced by resorption of parts of the shaft, cortex or ends of the bones and their replacement by connective tissue, and the formation of new bone at the end of the metaphysis and under the periosteum of the shaft (so called "layering" or "cloaking" of the periosteum). The epiphyseal end of the bone may be separated from the shaft, and as seen by X-ray this is usually a break in the end of the shaft rather than a true epiphyseal separation. Turnbull states that fibrosis is present in all but the slightest and earliest lesions, and that it is of great assistance in the macroscopic and microscopic recognition of syphilitic osteochondritis. In congenital syphilis, as in rickets, the ends of the long bones may be enlarged (fig. 574).

SYMPTOMATOLOGY

Snuffles; rashes.—It is the exception for a syphilitic infant who is born alive at term to show any obvious signs of the complaint. When signs are present at birth, such as wasting or a bullous rash, death generally ensues after a brief period. Usually at birth a syphilitic child appears well

nourished and blooming, but after three or four weeks it begins to waste and snuffles and a rash appears on the buttocks and forehead. Snuffling is one of the most constant features presented by an infant with congenital syphilis, and is due to swelling and excoriation of the nasal mucous membrane with a certain amount of viscid discharge. It leads to some broadening of the bridge of the nose which may, however, disappear as the child grows older. The more marked and permanent deformity caused by destruction of bone arises much later in the course of the disease, if it occurs at all. There is always some obstruction in the nostrils, and this may in rare cases be so great that the baby is unable to suck and has to be fed with a spoon. Accompanying the snuffles there is usually some laryngitis so that the infant has a hoarse cry. The skin rashes appear at about the same time, possibly a little before or after the snuffles, and they are frequently confined to the buttocks and genitals. They are usually erythematous in nature, and are similar in appearance and distribution to the rash produced in the delicate skin of many infants by the contact of alvine and urinary discharges. They tend, however, to spread farther down the thighs and legs and up on to the abdomen, and they are less bright, resembling more the colour of raw ham.

FIG. 575.—THE APPEARANCE OF THE FACE IN A SEVERE CASE OF CONGENITAL SYPHILIS.

The lips, chin (fig. 575) and brows are sometimes involved, and less frequently the palms and soles. The limited character of the distribution of these rashes affords a strong contrast to acquired syphilis, where the general roseola, almost unknown in the congenital disease, is the earliest and most typical of the skin eruptions. After the erythematous, papular rashes with some coarse desquamation, particularly of the palms and soles, are the most common, whilst vesicular and bullous eruptions are rare (syphilitic pemphigus). This condition is prone to appear at or shortly after birth in severely infected infants, and involves the palms and soles as well as other parts of the body. The prognosis in these cases, though better since the introduction of penicillin treatment, is grave. Associated with the skin eruptions there is generally loss of hair, not only on the head but also in the eyebrows. Some authors regard a profuse growth of hair—the so-called "syphilitic wig"—as a definite sign of the disease; this, however, is erroneous, as a similar appearance may be seen in children with no suspicion of a syphilitic taint and with a negative Wassermann reaction.

In gravely infected cases there may be inflammation of the matrix

of the nails and of the adjacent tissues (onychia and paronychia), as a result of which the nails atrophy and may be shed.

Sores about the lips are not infrequent, either in the form of mucous tubercles or more commonly as longitudinal radiating fissures or rhagades. These fissures give a characteristic appearance to the patient and are often followed by marked scarring, which in later life serve as a valuable diagnostic "stigma" of the disease. They should not be confused with the shallow ulcers at the angles of the mouth commonly seen in weakly children. Mucous tubercles may appear about the mouth and condylomata about the anus, but they are decidedly rare at this period, in contrast to their frequency and profusion in the acquired disease. The lymphatic glands may sometimes be found enlarged, but never to the extent observed in acquired syphilis in which their involvement is invariable.

Constitutional symptoms.—As might be expected, congenital syphilis often produces a marked effect upon the general nutrition of its victim. Wasting frequently occurs and in untreated cases may become extreme, the more so when the abdominal organs are affected, and any considerable degree of marasmus is a sign of serious import. Sometimes wasting is the only sign of a syphilitic taint in an infant, and a Wassermann test of mother and child may serve to establish the diagnosis: prompt anti-syphilitic treatment will in many cases save the child's life. A syphilitic infant often becomes anæmic, and the complexion takes on a characteristic whitish-brown hue—the so-called *café-au-lait* colour.

Epiphysitis.—It has been pointed out that changes at the epiphyses of the long bones occur in prematurely-born fœtuses and in infants dying soon after birth, changes said to be constant by some observers. Clinical signs of local or generalized syphilitic osteitis, periostitis, osteo-chondritis or epiphysitis, the name varying according to the character and distribution of the lesions as shown by X-rays, are not uncommon, but in many cases it is possible to demonstrate the lesion by X-rays before the patient manifests symptoms of epiphysitis. Clinical signs of osteitis may rarely be present at birth, or they may occur at any time during the few months of life, the majority of the cases starting from the fourth to the twelfth week. A child who has probably already had snuffles and a rash about the buttocks may seem to be in pain, and may be noticed not to move one or more of its limbs. Tenderness and swelling may be found about several of the epiphyses of the long bones, and in some cases one or more of the limbs may be apparently paralysed, the arms hanging motionless and flaccid, whereas the legs when affected are often in a condition of tonic contraction (Parrot's pseudo-paralysis). Occasionally this pseudo-paralysis may be the only symptom which a syphilitic infant exhibits when first seen by the physician. Neither pain nor tenderness is, as a rule, severe and may even be absent, and they seem insufficient to account for the pseudo-paralysis which so often accompanies epiphysitis. The arms are more often affected than the legs, and if loss of power occurs at or shortly after birth and affects the arm only, the condition may be erroneously diagnosed as Erb's paralysis. With appropriate treatment the

condition rapidly clears up, although in severe cases there may be separation of the epiphyses, and in rare cases there may be suppuration in the joint.

Syphilitic pseudo-paralysis has also to be distinguished from scurvy, infantile paralysis, and acute epiphysitis and osteomyelitis. Scurvy is rare before the age of six months, whereas the paralysis of syphilis generally occurs in the second or third month after birth, and is uncommon after six months. Pain and tenderness, as well as local swelling, are more pronounced in scurvy. The presence or absence of other signs of the complaints, the X-ray appearances and the Wassermann reaction of mother and child, will usually establish the diagnosis. Infantile paralysis is also rare at the early age when epiphysitis is most likely to arise. Its onset is more sudden and is followed by rapid degeneration of the affected muscles with an early reaction of degeneration to electrical stimulation, and there is an absence of tenderness or swelling in the epiphyseal regions. The intense pain and tenderness, and the marked constitutional symptoms, are usually sufficient to render the diagnosis of "acute" epiphysitis, easy.

FIG. 576.—SYPHILITIC OSTEOMYELITIS AND PERIOSTITIS FROM A CHILD AGED TWO MONTHS.

Note the characteristic loss of cortex and rarefaction at the upper and inner aspect of the tibia; also the marked periosteal splinting or cloaking.

In a case at The Hospital for Sick Children, there was marked swelling and tenderness of the upper half of the right tibia in a child aged two months, who exhibited no other symptoms suggestive of congenital syphilis. The child was not obviously ill, the temperature between 99° and 100° F., the leucocytes were 8,000 to 10,500 per c.mm. and a blood culture was sterile. Clinically the condition was considered to be one of acute osteomyelitis, but a positive Wassermann and Kahn reaction together with the X-ray appearance and the site of the lesion established the diagnosis of congenital syphilis (see fig. 576).

The condition improved considerably under anti-syphilitic treatment, but the child unfortunately developed gastro-enteritis which proved fatal.

It is rare for syphilitic osteo-periostitis to attack the bones of the hands and feet. Syphilitic dactylitis usually begins in the proximal phalanges of the fingers or toes, and may then implicate the metacarpal or metatarsal bones. Several of the fingers or toes may be affected and clinically the digits show a rather characteristic skittle- or flask-shaped appearance. Syphilitic dactylitis rarely, if ever, occurs without osteitis or periostitis of some of the other long bones in the body, and very rarely suppurates or necroses.

Cranial manifestations.—There are certain alterations in the skull which have been regarded as being of purely syphilitic origin. Of these, craniotabes or thinning of the bones so that they dent easily on pressure, is by no means confined to syphilitic babies, though more frequent in them. It occurs especially in the occipital bone and the posterior portions of the parietal bones, and it is due to irregular ossification with resulting islets of unossified membrane. Parrot's nodes—thickenings of the bones around the anterior fontanelle—give rise to the " natiform skull " or " hot-cross bun " appearance. This is to be regarded as significant only if present before the end of the first year, because later on it may be complicated and somewhat masked by the frontal and parietal bosses of rickets. A slight or mild degree of hydrocephalus, resulting from syphilitic meningitis, may also be met with in early life, giving rise to a large head with prominent frontal and parietal eminences.

Visceral lesions.—The viscera are much less frequently attacked in infants born healthy and who show the first signs of syphilis at four or six weeks of age than in those who die before or shortly after birth. In the latter the spleen, kidneys and liver are often affected, the symptoms including ascites, possibly jaundice, albuminuria and a proneness to hæmorrhages. In the former the spleen is enlarged to a varying degree in the majority of cases, the liver is sometimes enlarged and in rare cases there is a painless enlargement of the testicles.

Blood changes.—There is no characteristic blood picture associated with congenital syphilis, but various types of anæmia may be met with. The most common is the more or less normochromic anæmia of infection. Some of the cases which would previously have been diagnosed as von Jaksch's anæmia, pseudo-leukæmia infantum, are syphilitic, but the leucocytes show no constant qualitative or quantitative changes. Rarely, in severely infected infants, there may be an erythroblastosis.

In syphilitic infants and children the erythrocyte sedimentation rate is usually high before treatment is begun. It may be as much as 50 mm. in one hour in a 100 mm. column of blood, as tested by Payne's method (Payne, 1932). During treatment the rate approaches the normal 3 to 10 mm.

Neurosyphilis.—On systematic examination of the cerebrospinal fluid of syphilitic infants evidence is frequently found of involvement of the central nervous system. The fluid may be slightly opalescent from the presence of cells, it may contain an increased amount of albumin and globulin, and it may give a positive Wassermann reaction and colloidal-gold (Lange) curve. Some of these patients may exhibit no symptoms referable to the central nervous system (latent neurosyphilis), and as a rule the pathological changes in the fluid disappear as a result of anti-syphilitic treatment, so that on subsequent examination the fluid appears normal. Other patients may have obvious signs or symptoms (clinical neurosyphilis), such as convulsions or true epileptic fits ; bulging of the fontanelle, stiffness of the neck and some hydrocephalus, due to a subacute or chronic meningitis ; mental deficiency or idiocy. When the spinal fluid is re-examined in such cases, it will again show evidence of a patho-

logical condition, and it is highly probable that some of these patients are candidates for juvenile general paralysis, hemiplegia and other dire results of syphilitic meningo-vascular disease, and premature death unless they are treated early and intensively.

Special sense organs.—The eyes are attacked in a large proportion of infected infants, generally in the form of disseminated choroiditis, though iritis and, rarely, optic neuritis and interstitial keratitis may occur even at the tenderest age. With choroiditis the vision is not obviously affected, and the condition may only be detected by a routine ophthalmoscopic examination.

Relapses.—Unless adequately treated in infancy manifestations of congenital syphilis tend to return after their first disappearance, but the phenomena of a "relapse" differ markedly from those originally present. A recurrence of rashes or of pseudo-paralysis is rare, the relapse being usually indicated by snuffles and by mucous tubercles about the mouth and anus. After the age of twelve months condylomata are not uncommon, and when situated, as they usually are, around the anus, the child is not infrequently brought to the doctor on account of "piles."

LATER MANIFESTATIONS

Bones.—After about the third year of life symptoms begin to appear which may be compared with what are called "tertiary symptoms" in acquired syphilis. Thus nodes may appear on the bones and gummata in the skin, liver, lungs and more rarely in other organs of the body. In the absence of treatment these tend to break down, producing abscesses and ulcers, with destruction of soft tissues and even bone. Marked deformities may thus arise, among the most frequent being perforation of the palate and nasal septum with, in the latter case, a sinking in of the bridge of the nose. Periosteal thickenings may deform the long bones and skull, and the tibia—the bone most frequently affected—becomes specially characteristic, the shin being bowed forward like a cutlass or sword (sabre tibia). Pain in the limb, usually more marked or in some cases felt only at night when in bed, is the symptom complained of. There may be enlargement of the limb in these cases, and the diagnosis may have to be made from

FIG. 577.—SYPHILITIC OSTEO-PERIOSTITIS IN A BOY, AGED EIGHT YEARS.

tuberculosis, sarcoma and osteomyelitis. The Wassermann reaction and X-ray appearances will help to make the diagnosis, as also in syphilitic dactylitis which has to be differentiated from the tuberculous variety. In tuberculosis there is swelling about one or more of the proximal phalanges or about the affected tibia, which frequently goes on to ulceration and bone destruction. In syphilis there is much deposition of periosteal new tissue which, as a rule, goes on to calcification and sclerosis, and only occasionally softens and breaks down. In the rachitic curvature of the tibiæ which sometimes occurs, the bones are actually bent, particularly in their lower third, whereas in syphilis the forward curve of the anterior edge of the tibia may affect the whole length of the bone, and is due to the deposition of new bone along the anterior part of the shaft (fig. 577).

Joints.—A painless, usually symmetrical, effusion involving most commonly the knee joints (" Clutton's joints ") is a not infrequent manifestation of late congenital syphilis. This condition may arise at seven or eight years of age, but is usually seen at a somewhat later period of childhood. As a rule there is no concomitant bony lesion, so that in a skiagram only an abnormal separation of the articular surfaces is seen. If there be an associated osteitis or epiphysitis, the patient may complain of pain and the swollen joint may feel hot, with the result that the condition may be diagnosed as rheumatism or as tuberculosis. A rarer form of arthritis occasionally met with in syphilitic children is one which simulates rheumatoid arthritis, with thickening of the periarticular tissues and, in some cases, synovitis with possibly osteophytic formations.

Teeth.—The deciduous teeth do not show any changes which can be regarded as pathognomonic of congenital syphilis. It is the changes seen in the permanent teeth—and in particular the upper central incisor teeth—which were first described by Jonathan Hutchinson and are hence known as Hutchinsonian teeth, which are characteristic of congenital syphilis. In its typical form the Hutchinsonian incisor is small, tapering, with a rounded anterior surface and a well-marked central notch in the cutting edge (fig. 578). Occasionally the lateral incisors and rarely the canines may present a similar, but less pronounced, appearance. The lower incisors are frequently small, perhaps slightly tapering, and may have a convex anterior surface with a small notch in the cutting edge like the upper teeth; or they may be widely spaced and set like " tombstones " in the gums. The six-year-old permanent molars may also present an appearance which has a high diagnostic value. Moon, who described them in 1877, called them " dome-shaped," a name which draws attention to the tapering of the crown of the tooth; they have also been called " mulberry " molars owing to the fact that the cusps, instead of being well-formed and cone-shaped, are stunted and rounded. The statement of Sabouraud that the " tubercle of Carabelli," so often present on the upper six-year-old molars, is a sign of congenital syphilis has been entirely discredited.

The typical Hutchinsonian incisors and Moon's molars are by no means always present in cases of congenital syphilis—probably in only

25 or 30 per cent. of the patients over seven years of age—but when present they are diagnostic of the disease. It should be noted, however, that congenital syphilitic patients often show less pronounced changes than those just described, such as a narrowing towards the cutting edge but no notch (the " oat-shaped " tooth), and these should always arouse suspicion and stimulate further investigation of the case. That the notch in the typical Hutchinsonian tooth is not invariably produced by attrition of a thinned cutting edge, is proved by the fact that by X-rays it can be demonstrated in the unerupted tooth *in situ* in the jaw.

FIG. 578.—HUTCHINSONIAN TEETH IN A CASE OF CONGENITAL SYPHILIS, SHOWING THE NARROWED AND NOTCHED UPPER CENTRAL INCISORS, AND A SIMILAR NARROWING WITH SUGGESTION OF NOTCHING IN THE LOWER CENTRAL INCISORS.

Sense organs.—In late congenital syphilis the eyes are frequently attacked, but at this period it is the cornea which suffers, whereas in early life it is usually the choroid. The inflammation of the cornea, interstitial keratitis, is manifested by a varying amount of pericorneal vascular injection, and by the cornea itself becoming opaque, giving rise to a ground-glass appearance. When the inflammation is at its height areas of dilated capillaries spread from the edge into and over the cornea giving rise to the so-called " salmon patches." Photophobia is a marked feature of the condition. Both eyes are usually affected and with proper treatment the corneæ clear up well, but occasionally a slight nebula may persist. At times relapses may occur even while the patient is being energetically treated, hence the view held by some authorities that interstitial keratitis is an allergic manifestation of congenital syphilis. It is by far the commonest symptom of late syphilis (" lues congenita tarda ") and affects girls more frequently than boys.

The ear may also be implicated, the auditory nerve being the part that suffers. The patient becomes gradually or sometimes suddenly deaf and the deafness once established is as a rule permanent. Fortunately,

as a result of the modern methods of treating the disease, deafness is a far less common symptom than it formerly was.

The notched and pegged incisor teeth, interstitial keratitis and deafness were stressed by Hutchinson as the three cardinal signs of late congenital syphilis and are hence known as the " Hutchinsonian triad." The first two are frequently seen in association with one another, but the triad is rare.

Neurosyphilis.—The lesions of the central nervous system in late congenital syphilis are substantially the same as those met with in the acquired disease in the adult. At times they are surprisingly limited in extent, for example to a single cranial nerve, resulting in the loss of the pupil reflex or a squint or optic atrophy or nerve deafness. In a series of cases at The Hospital for Sick Children all of the following have been seen :—meningitis and meningo-encephalitis, spastic diplegia and paraplegia, cerebral vascular disease, juvenile general paralysis, tabes and taboparesis, epileptiform seizures and various degrees of mental deficiency and deterioration resulting from congenital neurosyphilis. Sometimes unequal pupils may be the only sign pointing to meningeal disease, and headache the premonitory symptom of disease of the cerebral arteries. In all the above-mentioned cases the blood Wassermann will almost invariably be found positive, and the cerebro-spinal fluid generally so. The spinal fluid may show in addition an increase in the albumin and globulin content and in the number of cells present, while the colloidal-gold (Lange) curve may be of the luetic or of the paretic type.

In milder degrees of involvement of the central nervous system, the symptoms may be an excessive nervous irritability, some mental retardation, undue naughtiness and even downright delinquency ; on the other hand some of these children may show marked mental precocity. In addition, there may be latent or asymptomatic cases which have been well treated in childhood, whose blood and cerebro-spinal fluid still give a positive Wassermann reaction and whose fluid is abnormal in other respects. Possibly these are the cases which develop into juvenile general paralysis and tabes, unless modern treatment is carried out. It has often been suggested that there is a special neurotropic strain of the treponema, so that if one or other parent has tabes or general paralysis the child is likely to have neurosyphilis. When such a family history is obtained it is important to examine the child's cerebro-spinal fluid, even if there be no obvious involvement of the central nervous system.

Whilst not wishing to imply that all or even a large proportion of feeble-minded, deficient or mentally backward children are syphilitic, it is strongly advised that a blood test be done on both mother and child, and that careful inquiry be made into the history of every case of mental deficiency, because these patients, if syphilitic, sometimes respond in a striking manner to anti-syphilitic treatment.

Other symptoms.—In the absence of efficient treatment congenital syphilitic children are often under-sized, ill-nourished and sallow-complexioned or anæmic, so that their resistance to other diseases, notably infections, is lowered. There may be some enlargement of the lymph nodes (post-cervical, epitrochlear, inguinal) and in a few cases a group of

enlarged cervical glands may be the presenting symptom. No other cause than syphilis could be discovered, the Wassermann reaction was positive in each case and the glands disappeared under anti-syphilitic treatment. Late congenital syphilis may affect the liver in the form of cirrhosis or gumma ; the kidneys, producing a form of chronic nephritis ; and the lungs, larynx and bronchi in which fibrosis or gummata may occur. The spleen is not infrequently enlarged, especially while the disease is still active. The heart and large blood-vessels are occasionally, but very rarely in childhood, affected by the changes which are so common in the acquired disease. Paroxysmal hæmoglobinuria in children is almost always due to congenital syphilis and is rapidly cured by specific treatment.

DIAGNOSIS

The diagnosis of congenital syphilis in its early or later stages is often a comparatively simple matter provided the possibility of its occurrence is borne in mind, and whenever the disease is suspected serological tests of both mother and child should be taken. If the case is clinically syphilitic, such tests will serve to confirm the diagnosis, and will also be useful as initiating a series of blood tests which will be necessary before finally regarding the patient as cured ; on the other hand, if the diagnosis is in doubt positive serological tests will dispel the doubt. It is advisable in all cases to supplement the Wassermann test with the Kahn test or some other flocculation test (Sachs-Georgi, Meinicke, Kline, etc.). A single negative Wassermann reaction is not conclusive evidence against syphilis, for the reaction may show intermissions even in the absence of treatment, and children may be encountered who are clinically syphilitic or are members of a syphilitic family, but nevertheless give a negative reaction. Rarely the mother of a syphilitic child may herself have a negative Wassermann reaction. If a mother's blood test is negative and the child's positive, the tests should always be repeated to ensure that no technical or other mistake has been made, and it must be remembered that certain dermatoses, such as eczema or psoriasis, may sometimes give rise to a false positive Wassermann reaction. There are one or two other reservations to be made in the case of very young children : (1) A positive reaction in a symptomless child less than two months old is not necessarily evidence of syphilis in the child. It may be due to the transference of the Wassermann reagin from the mother, and at subsequent testings the child's blood may become and remain negative, and the child never show any signs of syphilis. (2) A child may give a negative test at birth and during the first few months of life and become positive later with the onset of symptoms. When the symptoms suggest an involvement of the central nervous system, such as hydrocephalus, fits, or mental deficiency, an examination of the cerebro-spinal fluid should invariably be made. Cases of congenital syphilis are not infrequently missed through the omission to do tests on the blood or spinal fluid, with the lamentable result that months or even years of valuable time are lost to the detriment of the patient's future well-being.

On the other hand, there is the danger of diagnosing every rash in infants as syphilitic, especially by the inexperienced.

With a typical rash and rhagades about the lips the complaint may be recognized at a glance, but the signs are not always so distinctive. The rash will have to be differentiated from the erythematous condition produced in the ano-genital region by the irritation of urine or fæces. In syphilis the eruption has a coppery colour, and tends to spread as discrete maculæ over the front of the abdomen and below the thighs to the legs. The presence of a rash about the mouth, chin, nose, eyes and forehead, and especially on the palms and soles would strengthen or establish the diagnosis. Snuffling is an important and almost constant feature of congenital syphilis, but it is quite common in infants from other causes. A history from the mother of several miscarriages or of previous children afflicted with snuffles and rash may suggest that a marasmus is of syphilitic origin. An ophthalmoscopic examination is of considerable value, as choroiditis is a frequent early manifestation. Pseudo-paralysis has to be differentiated from Erb's paralysis, infantile paralysis, acute epiphysitis and osteomyelitis, and from scurvy, and its distinguishing features have already been emphasized. After the first year condylomata about the anus should be looked for in cases of suspicion, and in later childhood and adolescence, given an obscure lesion which is not obviously due to some other cause, inquiries and tests as to the possibility of syphilis being the cause should be made. Among such " obscure lesions " may be included affections of the bones and joints, liver and kidneys, unexplained anæmia, hæmoglobinuria and under-development of body or mind. In addition to inquiry into the family history—of grandparents as well as parents—an investigation of the patient for the stigmata of congenital syphilis should be made and will sometimes provide evidence of the disease. Such stigmata are a mild hydrocephalus with frontal bossing, saddle-shaped nose, scars about the mouth and chin, varying degrees of Hutchinson's teeth, Moon's molars, corneal nebulæ, perforation of the palate with scarring of the faucial and pharyngeal region, and " sabre " tibiæ.

PROGNOSIS

In addition to the heavy pre-natal mortality resulting from syphilis, a number of infants die shortly after birth, especially if born with syphilitic pemphigus or marasmus. The prognosis as regards life is good as a rule if the symptoms are late in appearing, if the infant is breast fed and its general condition can be maintained ; the prognosis is better if the mother has had some treatment during pregnancy, and if the child's treatment is begun early and is conscientiously carried out with due regard to hygienic and general conditions. Children of syphilitic parents born further removed from the date of infection are, as a rule, less severely infected than the older children, but this is not invariably the case.

On the other hand, varying degrees of permanent disability may result from early choroiditis, interstitial keratitis, ulceration of the palate with

perforation, lesions of the liver, kidney and other glandular organs, from affections of the ear and, above all, from lesions of the central nervous system. Paralyses, mental defects, juvenile tabes and general paresis are the possible sequelæ to the vascular, meningeal or parenchymatous syphilitic degenerations which may occur in the congenital disease. Syphilitic children are more prone than healthy children to die from other affections, but this applies rather to early and untreated cases than to those which have received energetic treatment.

PREVENTION

Parental syphilis has long been recognized as a potent factor in the ante-natal death of the fœtus. The age of the infection in the father and the amount of treatment he has received before the conception of the child, generally have an influence upon the severity of the child's infection, for if the disease in the father be more than ten years old and especially if he has had adequate treatment, the child may—and indeed probably will—be born free from the syphilitic taint. Should, unfortunately, the child be born infected, it will have only a mild early infection or, failing this, exhibit one or other manifestation of "lues tarda." With the mother, however, the case is different. Even if she give no history and show no signs of the disease, she may none the less be suffering from latent syphilis, with in most cases a positive Wassermann reaction, and if untreated may at any time, even twenty years afterwards, give birth to a syphilitic child. Congenital syphilis can be almost entirely prevented by the routine blood testing of all expectant mothers and treating those who give a strongly positive reaction. Where this safeguard has been adopted congenital syphilis has been almost eradicated (Wattie, 1944; Nabarro, 1944). It must, however, be emphasized that one positive serological test in a pregnant patient is not by itself justification for a diagnosis of syphilis. A detailed history should be taken and a careful clinical examination made, together with repeated serological tests before treatment is begun. Some pregnant women found to give positive blood tests are themselves cases of congenital syphilis. Before the advent of penicillin therapy, treatment consisted of repeated courses of arsenicals and bismuth and, provided such treatment could be given from the early months of pregnancy to term, results were good. Now penicillin has replaced arsenic and bismuth to a great extent, and has the obvious advantages of speedy administration and comparative freedom from ill-effects. Penicillin is transmitted through the placenta from the earliest week of its formation, and American authorities claim that the results of treatment in pregnancy by penicillin alone are better than those following the use of arsenic and bismuth. It is too early to be dogmatic about the use of penicillin alone, and many venereologists in this country would, in cases of acquired syphilis in pregnant women who have had no previous treatment, advocate penicillin followed by arsenic and bismuth.

It has been the practice, and still is, to give treatment in subsequent

pregnancies even when the mother has had full anti-syphilitic treatment and tests of cure ; in America a series of 221 such women were not given any active treatment in pregnancy and only one congenital syphilitic child was born (Thomas, 1949). Again it is too early to conclude that treatment in pregnancy of a previously treated syphilitic woman can be omitted ; what can be said in these cases is that, provided serological tests remain consistently negative, a course of penicillin early in pregnancy with a second course in the last six weeks of pregnancy should ensure the birth of a child free from syphilis.

THIRD GENERATION SYPHILIS

Whilst some authorities deny the possibility of syphilis being transmitted to the third generation, many admit that there is no valid reason why a congenitally syphilitic woman, who has not received anti-syphilitic treatment, may not bear a syphilitic child by a healthy father. The thesis of " third generation syphilis " is almost impossible of scientific proof, owing to the difficulty in most cases of establishing the absence of syphilis in the father. Nabarro (1933), during the course of twenty-two years' experience in the venereal disease clinic at The Hospital for Sick Children, came across thirty or more families members of which had syphilis in three generations. In two families both parents were congenital syphilitics ; one mother who had been treated in childhood bore a healthy child, whereas the other mother who had not received any treatment bore a syphilitic infant. A congenitally syphilitic expectant mother should be treated as early as possible in her pregnancy, if she has not previously received adequate treatment.

TREATMENT

Early congenital syphilis.—Once the diagnosis has been established treatment should be begun as soon as possible ; the earlier treatment can be given the better is the chance of negative serological tests being obtained, and treatment initiated before the sixth month of life results in negative tests in nearly 100 per cent. of cases. Penicillin has very largely replaced the older treatment by arsenic and bismuth and results obtained so far, though not conclusive, are such that it seems unjustifiable to employ the more difficult and dangerous forms of treatment.

Several American investigators (Moore *et al.*, 1944 ; Lentz *et al.*, 1944 ; Platou *et al.*, 1944, 1947 ; Ingraham *et al.*, 1946 ; Yampolsky and Heyman, 1946) have recorded results of the treatment of syphilitic infants with penicillin alone.

In the aggregate 252 infants were thus treated and the short-term results were fully as good as, and in some cases better than, those following the older methods of treatment with arsenic and bismuth. Twenty-seven deaths from all causes (10·7 per cent.) occurred amongst the patients treated, but many of them were from intercurrent disease and nineteen of the twenty-seven deaths occurred in infants who were three months or younger when treatment

was begun. The dosage of the drug has varied within wide limits, the tendency in the earlier observations being to give too small doses, for example, a total of 20,000 units per kilogramme body-weight (Moore), the equivalent of 1,200,000 units in the adult. Lentz gave double this dose and since a severe reaction occurred in one case, he recommends a reduced dosage for the first two or three days. Ingraham and his associates found that a considerably larger daily dose of penicillin continued over a longer period gave the best result. One infant, aged five weeks, was given a total of 74,000 units per pound body-weight for fifteen days, the equivalent of 11 million units for an adult. Yampolsky and Heyman during their investigations increased the dosage from a total of 40,000 to 50,000 units per kilogramme body-weight in their earlier cases to 100,000 units per kilogramme in the later cases. This amount was given in equally divided doses every three hours intramuscularly over a period of ten days. In view of the fact that early brands of penicillin contained " impurities " which may possibly have been responsible for some of the beneficial effects attributed to penicillin itself and that available samples of the drug are more highly purified than was the older penicillin, these authors recommend that the dose should be at least doubled to maintain its efficacy in the treatment of congenital syphilis. In their report of 1947 which is based upon the combined results obtained in five co-operating clinics in the U.S.A., Platou and his associates offer the following suggestions for the treatment of congenitally syphilitic infants : a total dosage of at least 100,000 units per kilogramme body-weight given in 120 approximately equal intramuscular injections over twelve to fifteen days. The injections should be given at intervals of not more than three hours around the clock.

The immediate response of early congenital syphilis to penicillin therapy is gratifying. Lesions showing treponemata by darkground illumination become negative within twenty-four hours of starting treatment. Cutaneous and mucous membrane lesions have healed during or shortly after treatment. Rhinitis clears in from two weeks to two months. X-ray evidence of the characteristic osteo-chondritis has disappeared in from two to six months. Regression of liver, spleen and lymph node enlargement was usually complete by three months. Abnormal spinal fluid findings improved remarkably after treatment. Most sera became negative between the fourth and twelfth months after the course of injections. There were six clinical relapses (2·4 per cent.) ; these occurred as early as three months or as late as eleven months after initial therapy. The cases that relapsed were treated again with two or more times the original dosage. The results in 141 living infants observed from 60 days to 480 days after treatment were 116 satisfactory, seventeen unsatisfactory, and eight uncertain. Better results were recorded after bigger dosages—89 per cent. satisfactory after 40,000 or more units per kilogramme as compared with 74 per cent. after less than 40,000 units—though the follow-up periods after the larger doses have not been so long as after the smaller ones.

Newer preparations of penicillin are now being used instead of the aqueous preparations which have the disadvantage of necessitating frequent injections. Procaine penicillin G in oil with aluminium monostearate in doses of 150,000 to 300,000 units given daily or even on alternate days up to a total of 1,000,000 units is giving results comparable with those of the aqueous preparations. Following the initial course of treatment the child should remain under observation ; clinical and serological

examinations at frequent intervals are essential. If serological tests remain positive or if there is clinical or serological relapse further treatment is called for.

One negative test can never be accepted as evidence of cure and the observation suggested for infants treated for congenital syphilis is as follows :

(1) Clinical examination and serological tests monthly for six months.

(2) Clinical examination and serological tests at intervals of two months for a further six months.

(3) Clinical examination and serological tests at intervals of three months for a further year.

(4) Clinical examination and serological tests once a year until the child reaches the age of five years.

Many clinicians advocate that yearly observation should be carried out until growth has ceased, and while it must be admitted that relapse is always possible it is extremely rare after treatment. Whilst such prolonged observation may be regarded as ideal from a medical point of view it is not only exceedingly difficult to achieve but, in the later years, leads to family and social problems that cannot be disregarded.

The successful administration of penicillin to infants by mouth has been recorded (Henderson and McAdam, 1946). After 100,000 units had been orally administered, adequate concentrations of penicillin were present in the blood as long as twelve hours afterwards.

Some authorities ascribe toxic effects to penicillin. Lentz reported a severe reaction in one patient (out of nine treated) and on that account recommended reduced dosage for the first two or three days. Of Platou's 69 infants treated with penicillin, 34 showed reactions—mostly mild febrile attacks—on the first or second day of treatment ; but one infant developed severe, nearly fatal, collapse forty-eight hours after treatment was begun. Ingraham and associates state that debilitated infants may die in spite of penicillin and that 40 per cent. of the infants treated by them had toxic reactions—fever and severe gastro-intestinal disturbances, such as abdominal distension, loss of appetite, diarrhœa and occasional vomiting ; these symptoms, the authors add, might have been due to the disease itself. Yampolsky and Heyman, on the other hand, do not believe that reducing the earlier doses will prevent serious toxic effects, and consequently do not trouble to reduce dosage in the earlier stages of treatment.

Late congenital syphilis.—The term " late congenital syphilis " is usually taken to signify congenital syphilis manifest for the first time after the age of two years and in active cases the lesions are comparable with those of tertiary syphilis in the acquired form. Less is known of the results of treatment by penicillin alone in this stage and serological tests do not help in these late cases as much as in early congenital syphilis. In former years too much significance has been attached to a " positive Wassermann test " and it must be realized that many of these patients will have positive serological tests for years, if not for ever, after adequate treatment, just as the adult with late and latent syphilis. In brief, it

must be the patient who is treated and not the "positive Wassermann test."

The total dosage of penicillin should be increased in proportion to the body weight and the procaine penicillin with aluminium monostearate may be given in daily injections of 300,000 units to 600,000 units.

Many authorities still supplement penicillin treatment with injections of arsenic and bismuth in these late cases; when preparations of arsenic and bismuth are given the usual precautions must be observed and the doses graduated to the weight of the child.

Special mention may be made of interstitial keratitis, a condition almost exclusive to congenital syphilitics; opinion as to the most effective treatment of interstitial keratitis is divided, some advocate massive doses of penicillin, some fever therapy, some a combination of both. The use of arsenic does seem to hasten healing and the clearing of corneal opacities. Recently cortisone has been used as eye drops or subconjunctival injections with promising results.

As in early congenital syphilis children suffering from late congenital syphilis should be kept under prolonged observation and quantitative serological tests repeated. Finally, all children treated for congenital syphilis should have an examination of the cerebro-spinal fluid after treatment and, of course, at any time if neuro-syphilis is suspected.

The general treatment of the patient should follow the usual lines, but special care may be needed, for some mothers who are attending clinics for their own treatment do not also take their babies to infant welfare centres. As a rule the local manifestations of the disease do not require special treatment. The rash disappears rapidly with treatment. If there are many excoriations of the skin a boracic acid bath and gently drying the infant with a soft towel is a useful preliminary to treatment. The skin should be kept dry and well dusted. In these cases, and where there are anal condylomata, it is advisable to add some calomel to the dusting powder, *e.g.* a powder may be used consisting of equal parts of starch, zinc oxide, boracic acid and calomel. For the nasal catarrh which causes the snuffles, the nostrils should be mopped or irrigated with boracic acid or sodium bicarbonate lotion and then smeared inside with boracic ointment or a weak ammoniated mercury ointment (5 grains to 1 oz. soft paraffin). The ammoniated mercury ointment should also be used for sores about the mouth.

In the opinion of most syphilologists, children with latent congenital syphilis, that is to say, those discovered to have a positive Wassermann reaction in the routine investigation of a known syphilitic family, should be treated in order to safeguard them from the possibility of acquiring the serious later manifestations of the disease, particularly late neurosyphilis.

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VULVO-VAGINITIS IN CHILDHOOD

Definition.—An inflammation of the vulva and vagina in females between birth and puberty.

Types.—(A) Gonococcal. (B) Non-gonococcal.

Incidence.—From 1917 to 1928 inclusive the vaginal discharge was examined in 1,219 cases at The Hospital for Sick Children, Great Ormond Street. Of these 249 were regarded as being of gonococcal origin (20·4 per cent.), but this figure is probably too high as at that time the diagnosis was based largely on the examination of stained smears, which as will be shown later on tends to give a number of false positive results. During the succeeding ten years (1929–38) out of a total of 1,414 cases of vaginal discharge, 165 (11·7 per cent.) were of gonococcal origin, this lower figure more truly representing the incidence of the gonococcal cases as cultures in addition to smears were made from many of the patients. The London County Council in a special report (1938), summarizes the relative frequency of the two varieties of vulvo-vaginitis occurring during a period of two years among the many thousands of children—sick and healthy—under its care in thirty general hospitals, twenty special hospitals —children's, tuberculosis and fevers—20 residential schools and homes, and 15 nurseries for healthy infants. In all, 627 cases of vulvo-vaginitis were encountered of which only 32 (5·1 per cent.) were gonococcal. As the report admits, this figure underestimates the general incidence of the disease for known gonococcal cases would be diverted at once to the Council's special hospital for gonococcal infections and would never enter a general hospital. On the other hand, the Great Ormond Street figures are too high as the hospital had a venereal diseases clinic to which diagnosed cases were naturally sent. It will not be far wrong if it is estimated that 8 to 10 per cent. of the cases of vulvo-vaginitis in immature girls are due to the gonococcus. Practical experience leads to the conclusion that the shorter period of infectivity of adults which is believed to have resulted from the treatment of gonorrhœa with sulphonamides and penicillin, has reduced the incidence of gonococcal vulvo-vaginitis in children but there are no published records which either support or refute this suggestion.

Cohn and his collaborators (1942) in a three-year study in New York of 1,715 patients with vaginal discharge or who were contacts of infected persons, found 381 (22·2 per cent.) of the girls positive. It may well be that in different countries and in different parts of the same country, there are considerable variations in the incidence of gonococcal vulvo-vaginitis. The points to be emphasized are: (1) that the non-gonococcal cases far outnumber the gonococcal, and (2) that vulvo-vaginitis of immature girls is only very rarely a "venereal" disease.

Age incidence.—In the analysis of the Great Ormond Street cases both types of vulvo-vaginitis were found to be most common between the ages of two and five years. After that the gonococcal incidence fell markedly, but the non-gonococcal infections remained almost as numerous. Gonococcal infections were rare under the age of one year and the cases that did occur were due to small epidemics at another hospital. They were also rare between the ages of ten and twelve. Thus it would appear that liability to gonococcal infection is greater between the ages of two and five when exposure to infection occurs only in the home, than in older children when exposure to infection may occur both at school and at home. The London County Council report states that gonococcal vulvo-vaginitis is rarely met with at birth or during the first few weeks of life, because the vaginal epithelium is then of the adult type and the secretion highly acid, conditions which are inimical to infection with the gonococcus.

Seasonal incidence.—Both types of infection were found to be most numerous during the third quarter of the year. This may be due to the more scanty clothing worn in summer, or to a higher infection rate in adults at that time.

(A) Gonococcal cases

Ætiology.—Infection is contracted either directly or indirectly from another person suffering from gonorrhœa—directly, by assault or by infection from the mother during birth, both of which are rare; or by being in close contact in bed with an infected parent or another infected child. Direct infection by assault was found by Kathleen Brown (L.C.C. Report, 1938) to be the cause in 5 per cent. of 471 cases admitted to the Children's Medical Home, Waddon, between the years 1928 and 1936. Indirectly, the vulva may be infected by contaminated fomites, such as bed linen, towels, sponges or lavatories recently used by an infected person, or by being bathed with an infected child. Epidemics in hospital are due to these indirect modes of transmission as well as to lapses in nursing technique affecting nurses' aprons, bedpans, enema nozzles and clinical thermometers when temperatures are taken rectally. Several important maxims must be borne in mind in this connection: (1) Adults suffering from gonorrhœa should be warned of the danger of infection to children with whom they may come in contact. (2) Strict nursing precautions must be taken in a vaginitis ward or if a case of vulvo-vaginitis is being nursed in a general ward. (3) The parents and sisters of a gonococcal vulvo-vaginitis patient should, if possible, be examined for the presence of gonorrhœa; a brother or lodger might be the source of infection by soiling a lavatory seat or in some other more direct way.

Incubation period.—The period usually stated is three to four days but the limits may be from one to eight days.

Signs and symptoms.—It is surprising how often, especially in older girls, vulvo-vaginitis may give rise to no symptoms, the patient being brought to the medical practitioner because a discharge is found on the underclothing. On the other hand, the child may complain of soreness or irritation of the vulva with a vaginal discharge, pain on walking and possibly also frequency of micturition and dysuria. The experienced clinician can frequently diagnose gonococcal vulvo-vaginitis on inspection alone. A profuse, yellow or greenish vaginal discharge, visible at the anterior end of the vulval cleft before the separation of the labia majora, is due to gonorrhœa. If the patient is ambulant the discharge is usually smeared all over the labia. The vulva may be inflamed to a varying degree and pus may be seen to ooze from the vaginal orifice with any expulsive effort the child makes. The discharge is occasionally blood-stained but is never so offensive as it is when there are foreign bodies in the vagina. In very early cases the discharge may be small in amount and watery. In neglected cases the labia and adjacent parts may be excoriated and covered with adherent crusts of dried pus. With the newer methods of treatment by chemotherapy chronic and relapsing cases are likely to become rare, but if they should occur the cervix should be examined for evidence of cervicitis.

Bacteriological diagnosis.—Even when clinically a case is undoubtedly of gonococcal origin it is advisable to take swabs of the vaginal discharge for the examination of smears and for culture. It cannot be too strongly emphasized that negative reports are frequently returned owing to the fact that the swabs have been taken by nurses or assistants who have not received the requisite special training.

On no account should an attempt be made to work single-handed: in the case of a placid child one assistant will suffice to hold the patient in the required position, but if the child is likely to be unruly or frightened a second assistant will be needed to hold her head and shoulders.[1] The child is placed on her back on a table with the knees flexed and the thighs held apart as far as possible without hurting the child, so that the vulva is exposed in a good light. The labia majora are separated near the posterior fornix by the nurse's gloved fingers. The vulva is then cleansed with a sterile wool or gauze mop soaked in sterile saline or, in an emergency, ordinary tap water. By getting the child to take a deep breath, spasm of the sphincter vaginæ will be relaxed so that a fine throat swab can be introduced without damaging the hymen. The swab must be passed well into the vagina and on withdrawal should have obvious discharge upon it. Two such swabs should be taken, one to make a thin, even spread on a clean microscope slide and the other to inoculate some special medium for the culture of the gonococcus. The inoculation may be made at once in the consulting room or the swab transferred as soon as possible to a laboratory for culture.

The "spread" slide is stained by Gram's method and in an acute case of gonococcal vaginitis characteristic intra-cellular, Gram-negative, bean-shaped diplococci are seen. They are uniform in size and some of the pus cells may contain as many as 20 or more pairs of gonococci. No other organisms are seen. In the very early stage, when the discharge may be small in amount and

[1] It is advisable to have the child's mother present in the consulting room.

watery, the gonococci are mainly extracellular, but they become intracellular as the disease progresses. In chronic cases, other organisms, such as Gram-positive cocci and Gram-negative bacilli may be present either alone or in association with doubtful gonococci, and it is in these cases that examination by culture is so important. Without the aid of cultures the tendency will be to diagnose gonococci when they are not present, and this mistake is not infrequently made, for it is not uncommon to find intracellular short *B. coli* and even Gram-negative short-chained streptococci simulating gonococci, but, unlike the gonococcus, varying in size. In doubtful cases films and cultures should be made on at least three occasions.

For the cultivation of the gonococcus various media are recommended such as, " chocolate " agar (Carpenter, 1943), digest agar with defibrinated blood (L.C.C. Report, 1938) and others. These are poured into Petri dishes as required, and the poured plates evenly inoculated with the charged swab. Incubate ærobically at 36° or 37° C. for 24 to 48 hours. It will then be possible to identify likely gonococcus colonies with a lens—they are greyish, translucent, roughly circular and with a wavy outline. Such a colony picked off, emulsified with water on a slide and stained by Gram and counterstained, shows the gonococci as Gram-negative, kidney-shaped diplococci varying somewhat in size. (In smears of the original pus, as stated above, the gonococci are uniform in size.) This evidence is sufficient for all practical purposes, but to confirm the diagnosis and in particular if there should be any possibility of legal proceedings in connection with the case, confirmatory tests should be carried out : such as McLeod's oxydase reaction, sugar fermentations and cultivation on ordinary agar at room temperature under which conditions the gonococcus fails to grow.

The *gonococcal complement fixation* test plays little part in the early diagnosis of vaginitis in children and its value as a test of cure is still uncertain. Proven cases of gonococcal vulvo-vaginitis have been seen with negative complement fixation test throughout the attack.

Complications.—These depend on local or metastatic spread. The neighbouring orifices of the anus and urethra may become infected and subsequently act as foci from which reinfection of the vagina may occur. The percentages of anal infections given by different authorities show wide variations, for example Cohn and his co-workers (1942) state that 45 per cent. of the 381 children in their series had positive rectal cultures at some time during the course of their gonococcal infection, though on proctoscopic examination none of the children showed evidence of proctitis. At the Children's Medical Home at Waddon, Kathleen Brown (L.C.C. Report, 1938) records 11·8 per cent. with proctitis. In the clinic at Great Ormond Street positive cultures were obtained in about 20 per cent. of the cases, but there was no evidence of proctitis. The swabs were taken through a small speculum after careful cleansing of the peri-anal skin. This is important since this area is bound to be fouled by the vaginal discharge and the rugæ may harbour gonococci which might give rise to false positive results. Urethritis as a complication of vulvo-vaginitis likewise presents somewhat of a problem. As has already been stated, frequency and pain on micturition may be early symptoms of the disease but urethritis is not common, for urethral infection was proved by culture in only a few cases. Among American authorities, Cohn *et al.* do not mention urethritis among the complications of vulvo-vaginitis, whereas Brunet and Tolle (1933) state that " the urethra is not often

involved and in this group of cases no special treatment was directed to this part." On the other hand, Kathleen Brown is stated to have found urethritis in 377 out of 467 (80·7 per cent.) of her cases at Waddon. It is undesirable to swab the urethral orifice in the acute stage of vulvo-vaginitis lest the infection be carried into the urethra, and fouling of its orifice with gonococcal pus might lead to an erroneous diagnosis of urethritis.

No infection of Bartholin's glands or of the periurethral tubules was found in the Great Ormond Street series of cases. Ascending infection to the cervical canal, endometrium, tubes and pelvic peritoneum may undoubtedly occur. This is more likely in children over two years of age. Brunet and Tolle (1933) stressed the importance of an endoscopic examination in all cases of vulvo-vaginitis, for no less than 80 per cent. of 175 cases thus examined showed some degree of cervicitis. Infection of the cervical canal, which produces no signs or symptoms, can be presumed when cases resist treatment and relapse repeatedly after apparent cure, other sources of reinfection having been excluded. Occasionally we have seen pus exuding from the cervical canal on examination with a small glass vaginal speculum.[1] With the advent of modern treatment it is unnecessary and therefore undesirable to carry out routine examination of the cervix in early cases; it should be reserved for cases which resist treatment or relapse repeatedly. Infection of the pelvic viscera gives rise to pyrexia and abdominal pain which may be, and has been, mistaken for appendicitis, the more so as the vaginal discharge may be temporarily suppressed. In an untreated case less than a year old, gonococci were grown from the fundus uteri, after death from peritonitis had occurred. Metastatic complications are rare: one certain and one doubtful case of teno-synovitis, two of arthritis and one of dactylitis were encountered. There were no cases of iritis or other eye trouble, which is in agreement with the experience of other observers. It should be noted, however, that infants who suffer from gonococcal ophthalmia neonatorum may a few weeks later occasionally show signs of gonococcal vaginitis, though on account of the focusing of attention upon the more serious eye condition the vaginitis might be overlooked. The modern treatment of gonococcal infections with sulphonamide preparations or with penicillin will doubtless prevent the occurrence of most, if not all, of the complications enumerated above, including vaginitis following on ophthalmia.

Treatment.—Modern treatment by the administration of sulphonamide drugs or by penicillin has altered the concept of this disease. Formerly, when patients were treated locally by douches, packing and painting of the vaginal canal with antiseptic agents such as silver proteinate, tincture of iodine, chloramine, mercurochrome and many others, it was not uncommon to have a patient under treatment, as either an in- or an out-patient, for nine or even twelve or more months. Some improvement was effected by the administration of œstrin (Lewis, 1933; Nabarro and Signy, 1935) or of a synthetic œstrogen—stilbœstrol (Woodruff and TeLinde, 1942), either by mouth, by injection, or in vaginal suppositories. The giving of œstrin results in hyperplasia of the vaginal

[1] These were specially made by Messrs. Allen and Hanbury.

epithelium, so that it comes to resemble the adult type and in consequence the purulent gonococcal discharge rapidly gives place to a scanty dry, cheesy secretion often without visible gonococci and therefore much less likely to be infective to other children. The total duration of the disease was considerably reduced, but relapses frequently occurred.

It would appear from the observations of Cohn, Steer and Adler (1941), that the untreated disease undergoes "spontaneous cure." Forty-one untreated cases were used as controls to other forms of therapy and no less than 87 per cent. of them became negative, and remained negative by all tests, within twenty-eight weeks of observation : nearly 30 per cent. were negative at the end of five weeks and over 50 per cent. at the end of ten weeks. There were no recurrences of infection amongst these children. Presumably the chronicity of the disease so often noted formerly was not infrequently the result of the therapeutic measures employed, "strong antiseptics and vigorous local treatment, which probably delayed the healing processes of the tissues" (Cohn, Steer and Adler).

The sulphonamide group of drugs.—It appeared from early reports that of the sulphonamide group of drugs sulphapyridine and sulphathiazole were the most valuable, curing within a week 87 per cent. of seventy-seven patients treated (Rice, Cohn, Steer and Adler, 1941). Later researches by Satterthwaite, Hill and Huffer (1942) showed that sulphadiazine is much more bacteriostatic than sulphanilamide. The difference between sulphadiazine and sulphathiazole is not great but is slightly in favour of sulphadiazine. Of 100 adult gonorrhœa patients who completed treatment with sulphadiazine, 95 were completely cured.

The response to this form of chemotherapy was dramatic, and contrasted with long experience of the older forms of treatment in gonococcal vulvo-vaginitis, the results seemed almost miraculous.

A girl, aged nine years, was referred to the clinic at Great Ormond Street from another hospital which she had attended for nine days on account of a vaginal discharge. She had received no special treatment except sitz baths of potassium permanganate. When seen at the clinic the findings were typical of gonococcal vulvo-vaginitis and smears showed many pus cells and many characteristic intracellular diplococci. Culture yielded a practically pure growth of gonococci in twenty-four hours. Blood taken at the same time showed a negative gonococcal complement fixation test, also negative Wassermann and Kahn reactions. One tablet (0·5 gramme) of sulphapyridine was given as soon as the stained film had been examined and the diagnosis made. The following day *no gonococci were to be seen in smears*, which however, contained as many pus cells as did the previous ones. That day one tablet of the drug was given every three hours (2 grammes in all) and it was decided to stop treatment in order to ascertain if the small amount of the drug given (2·5 grammes) could effect a cure. (The patient was seen in December, 1938 before the dosage of the sulphonamides had been stabilized.) Smears, cultures and blood tests were taken over a period of seven months with repeatedly negative results. During the last five months of the period of observation the child was under the care of Dr. Kathleen Brown, at the Children's Medical Home at Waddon. It appears therefore from this record that as little as 2·5 grammes of sulphapyridine given in twenty-four hours was able to effect a cure of gonococcal vulvo-vaginitis in a girl of nine.

Subsequent observers (Rice *et al.*, 1941 ; Cohn, 1942 ; Lewis, 1943)

endorsed the effect of the sulphonamides; for example, Cohn and his co-workers write: "The response to chemotherapy is dramatic; all clinical symptoms of discharge, external irritation and inflammation subside rapidly, and smears and cultures become negative after 24 hours of treatment." The dosage recommended by them was 32 mgm. ($\frac{1}{2}$ grain) per pound body-weight daily, up to a maximum of 2 grammes (30·86 grains) daily in four equal doses. This treatment was continued for seven days and most of the cases responded to such a course; the few that relapsed were cured by a second course. Toxic reactions, such as rashes, conjunctivitis, headache and nausea may occur with sulphanilamide and sulphapyridine, but they are rarely met with when sulphadiazine and sulphathiazole are employed. Local treatment is unnecessary and indeed antiseptics of any kind are undesirable.

Penicillin.—Treatment by penicillin injection is now the treatment of choice and a single injection of 100,000 to 300,000 units given as procaine penicillin with aluminium monostearate will in most cases clear symptoms and ensure negative films and cultures within 24 to 48 hours. A few cases of apparent failure have occurred, some of which may have been due to inadequate dosage; up to the present time there is no evidence that penicillin-resistant strains of gonococci have developed.

Local treatment is limited to sitz baths and a dusting powder, and the fact that some authorities who apply antiseptics to the vagina and vulva report drug resistance and relapses would give support to the statement of Cohn and his colleagues referred to above, and to that of Lewis (1943) that strong antiseptics and vigorous local treatment probably delay the healing processes of the tissues.

Ross and his associates (1946) report the successful treatment of ten children with gonococcal vulvo-vaginitis and urethritis by the oral administration of penicillin. Doses of 100,000 units were given in double gelatin capsules hardened in formaldehyde-alcohol solution, every three hours for four doses. Adequate penicillin levels were maintained in the serum and all the cases were stated to have been cured.

An alkaline mixture is given if there is any dysuria. Rectal infection, if not cleared by the sulphonamide or penicillin therapy, is treated by running 1 to 2 oz. of a 2 per cent. silver proteinate solution into the rectum daily, this being retained for half an hour. Thread worms, if present, should be treated. Infections of the pelvic viscera are treated by applying hot fomentations to the hypogastrium with the possible addition of vaginal douching with warm saline solution. No case in the Great Ormond Street series required operation.

Administrative problems.—Until the advent of chemotherapy vulvo-vaginitis was the dread of those responsible for the administration of institutions in which little girls were being cared for, for in spite of all instructions to the medical and nursing staffs as to the precautions to be taken, lapses sometimes occurred with resultant epidemics in a ward. Nowadays patients with gonococcal vaginitis who require institutional treatment may be cared for in general wards, provided the usual isolation precautions which are applied in other communicable diseases are taken

(Cohn *et al.*, 1942; Lewis, 1943). In their view the disease does not spread from patient to patient but a fresh case results from the direct transmission of the discharge from an infective to a healthy child, usually through want of care in nursing technique. Treated patients are allowed to return to schools and institutions as soon as clinical signs have disappeared and cultures are negative; this usually means a period of a fortnight or even less. In this country, on the other hand, a more serious view is taken of the possible risk to other children partly no doubt because of legal actions which have been successfully brought by parents against public authorities, who by the alleged negligence of their staff have been held to be responsible for occasional outbreaks of gonococcal vulvo-vaginitis in hospitals. Should a discharge be found on admission to hospital the child should be at once isolated from other unaffected girls, pending a bacteriological investigation.

In dealing with any case of gonococcal vulvo-vaginitis in a child steps should be taken to induce the parents and other members of the household to be investigated (preferably at a special clinic) for the possible presence of a gonococcal infection. If such be discovered the infected individual must be persuaded to undergo treatment both for his or her own sake and for that of the other members of the household. If this course be not adopted and the affected child be treated as an out-patient or, having been hospitalized, be sent home soon after the discharge has ceased, she may become reinfected and such reinfection being regarded as a relapse, would be looked upon as a failure of the treatment which had been adopted.

Criterion of cure.—The disease is prone to relapse hence there should be a follow-up period of at least six months during which vaginal smears and cultures are taken at monthly intervals. Cultures should also be made at other times when suggestive clinical findings present themselves.

(B) Non-gonococcal cases

Ætiology.—Non-specific vulvo-vaginitis may be found associated with a variety of conditions, some general, others local. Among the general are (1) the acute specific fevers, in which a vaginal discharge may be a prodromal symptom as in measles or chicken pox; a sequela as in scarlet fever; or a complication which may occur during the course of the disease as in pneumonia or influenza; (2) in debilitating diseases and occasionally in anæmia; (3) secondary to throat infections, especially those of streptococcal origin; (4) pneumococcal peritonitis. The last-named have been recorded by some observers, but the writers have been unable to confirm their occurrence except as a rarity. Special cultural investigations were carried out in the Great Ormond Street clinic by Dr. Vida Perry in 1926-7 on all cases in which smears showed the presence of organisms resembling pneumococci. In every case the organism proved to be the *Streptococcus fæcalis*, which morphologically is often indistinguishable from the pneumococcus but, unlike the latter, is not bile-soluble. In 1931, Wood examined 71 consecutive cases of non-gonococcal vulvo-vaginitis in children aged one to eleven and a half years attending the clinic

at Great Ormond Street. The pneumococcus was found in only one patient, a girl aged six years. Locally there was nothing unusual about the case—there had been a small amount of whitish discharge for two years following " an attack of worms." The pneumococcus was of type IV and lethal to a mouse.

In this series of 71 cases examined by Wood, in addition to isolating the pneumococcus above described, he obtained the following results : 10 grew hæmolytic streptococci ; 51 other bile-insoluble streptococci ; in 19 anærobic Gram-positive cocci were found ; 24 grew staphylococci (2 *S. pyogenes aureus*, 1 in pure culture) ; 4 produced rods with the cultural characteristics of *Cl. welchii* ; 18 gave *B. coli communis* ; 18 gave non- or late-lactose fermenting bacilli ; and 5 gave various unclassified bacteria. Of Gram-positive rods, one case gave a non-virulent *C. diphtheriæ* ; 19 grew bacilli grouped by their fermentation reactions as diphtheroid, though distinguishable from the true Klebs-Loeffler bacillus by their colony formation, 26 as Xerosis and 9 as of Hoffmann type, while 2 were unclassified.

Among the local causes are (*a*) infection from the anal canal. Intestinal organisms may be conveyed by thread worms, lack of cleanliness and diarrhœa ; (*b*) direct infection from the mother's or nurse's fingers, clothing, or direct contact with dirt in the case of children who are inadequately clothed ; (*c*) irritation of the genitalia by tight clothing, by friction due to spasticity of the legs, and by masturbation. The last may itself be caused by a pre-existing irritation arising from eczema, glycosuria, hyperacidity of the urine, ammoniacal dermatitis, chronic constipation, thread worms, urinary tract infections and appendicitis ; (*d*) foreign bodies in the vagina, such as matches, cotton-wool or gauze swabs, hair-pins, safety-pins or buttons, all of which have been met with at different times.

Signs and symptoms.—In non-gonococcal cases the discharge is usually less in amount than in the gonococcal, and it varies in character according to the predominant organism present. It may be thin and watery as in streptococcal infections ; thick and creamy as with staphylococci ; thin and with an offensive odour when associated with *B. coli*. Pure diphtheroid infections produce little or no inflammation ; there is a slight opalescent discharge and the mucous membrane at the vaginal orifice has a pale translucent appearance. Foreign bodies when the cause of vaginitis practically always give rise to a diagnostic blood-stained, offensive discharge.

Bacteriological diagnosis.—Exactly the same technique should be employed in taking swabs for investigation as with gonococcal cases. Of the numerous organisms isolated by Wood, many were doubtless harmless saprophytes, but the commonest causal organisms were streptococci, *B. coli* and staphylococci. In fever hospital practice a hæmolytic streptococcus is the most likely organism to be encountered, as most of the cases of vulvo-vaginitis occur in connection with scarlet fever or streptococcal tonsillitis. Virulent and non-virulent strains of *C. diphtheriæ* may be isolated, but true diphtheria of the vagina is only rarely met with. In the opalescent discharge of girls approaching puberty the dominant and sometimes the only organism present is the large Gram-positive *B. vaginalis*

or Döderlein's bacillus. Trichomonas vaginalis infection in girls before puberty is rare but has been reported. Non-gonococcal vulvo-vaginitis has a very low degree of infectivity.

TREATMENT.—This depends on the cause and on the severity of the condition. Thread worms if suspected and found should be dislodged by appropriate treatment. If from the character of the discharge foreign bodies are suspected to be present, these should be looked for with a small glass speculum and, if found, should be removed by means of a long, narrow pair of forceps. Subsequent irrigation with chloramine (1 in 200), once or twice a day for a week, rapidly clears up the vaginitis. Masturbation, which may be a cause and may persist as a sequela, thus producing a vicious circle, must be controlled. Local cleanliness and tonics are indicated. In bigger girls when the discharge is slight, local treatment (beyond ordinary cleanliness) is best avoided, lest too much attention be drawn to the genitalia. In marked cases a lotion of chloramine (1 in 200), tincture of iodine (60 minims to a pint of water), or weak potassium permanganate solution (1 in 4,000) is recommended for bathing the vulva twice a day, and a dusting powder of zinc oxide and starch is useful for allaying irritation. Severe cases, especially those due to streptococci or staphylococci, should be treated with penicillin or sulphonamide drugs as recommended for gonococcal cases. Pure " diphtheroid " infections are of no significance and do not require to be specially treated. Baths, local cleanliness and tonics suffice.

Septic foci such as infected tonsils, sinuses or antra, carious teeth, pyelitis or cystitis should be appropriately treated. The majority of cases recover in two to three weeks, but it is advisable to follow them up for a few weeks longer as recurrences may occur. Over-treatment must be avoided, for this may prolong the vaginitis or even intensify it. Cases associated with septic foci are liable to be somewhat refractory even after the foci have been dealt with, doubtless owing to the child's lowered state of health. The parents should be warned of this fact.

Administrative.—Patients with a non-gonococcal vaginitis should be kept from school for ten to fourteen days, during which time appropriate treatment, repeated bacteriological investigations and a gonococcal complement fixation test are carried out.

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CHAPTER XXXV

INFECTIOUS DISEASES

H. STANLEY BANKS

SCARLET FEVER

Synonyms: Scarlatina: *Ger.* Scharlach.

Definition.—A syndrome associated with acute streptococcal tonsillopharyngitis or other local hæmolytic streptococcal lesion and characterized by toxæmia, a punctate erythematous rash, a mottled enanthem on the palate, faucial congestion and a red papillated tongue.

Modern conception of scarlet fever.—Scarlet fever comprises both a bacterial and a toxic element. The bacterial component is the reaction to the pyogenic or invasive activity of the hæmolytic streptococcus. This reaction usually consists of tonsillitis, faucitis, pharyngitis and may extend to inflammation of the middle ear cleft, cervical adenitis, rhinitis and sinusitis. The toxic component in the acute stage is shown by toxæmia, the rash, faucial congestion and papillated tongue and is due to the absorption of the soluble exotoxin (erythrogenic or Dick toxin) of the hæmolytic streptococcus. In extra-faucial (surgical, puerperal) scarlet fever, the hæmolytic streptococcus has its seat, not in the fauces, but in infected wounds, burns, genitalia or other focus and from this the erythrogenic toxin is absorbed. In addition to the local bacterial element there is sometimes a bacteriæmia. In the septic type, or *scarlatina anginosa*, which is associated with ulceration in fauces and pharynx, there may be septicæmia and pyæmia. In the toxic type, or *scarlatina maligna*, there is little local faucial reaction, but an overwhelming toxæmia and possibly also septicæmia.

Scarlet fever should not be regarded exclusively as an acute specific infectious disease *per se*, like cholera or plague. The hæmolytic streptococcus from one case may reproduce an entirely different clinical picture in another case, *e.g.* tonsillitis, acute rheumatism, nasopharyngitis, otitis media, adenitis, sinusitis or pneumonia. Conversely, the organism concerned in these and other clinical manifestations of streptococcal activity may, by transference to another case, give rise to scarlet fever. Thus, scarlet fever is but one of many clinical manifestations of acute hæmolytic streptococcal infection. Its characteristic, distinguishing feature is the punctate rash and, broadly speaking, it occurs only in individuals (Dick-positive reactors) who are susceptible to the rash-producing action of the exotoxin. Moreover, the capacity to produce scarlet fever is not confined to a single specific organism. All thirty Griffith types of human pathogenic hæmolytic streptococcus have been found capable of producing scarlet fever in susceptible subjects, but certain of them do so very rarely (Schwentker, Janney and Gordon, 1943).

Epidemiology.—Factors such as race, age, climate, season, clinical severity are associated with: (1) communicability and virulence of hæmolytic streptococci and (2) reactivity of the skin to the erythrogenic toxin. Communicability is favoured by aggregation of susceptibles, *e.g.* in schools, dormitories or hospital wards, especially during the colder weather when ventilation tends to be faulty. Reactivity of the skin nearly always depends on whether the erythrogenic toxin is neutralized or not by antitoxin present in the blood, that is, it is a function of immunity. There are, however, some exceptions in which the lack of skin reaction may be a function of the skin itself rather than of immunity. Infants under six months do not usually react to the Dick test and rarely, if ever, contract scarlet fever. Yet Cooke (1928) was unable to demonstrate antitoxin in the blood of such infants. Although, therefore, they are insusceptible to scarlet fever they cannot be said to be "immune" in the serological sense. Individuals living in tropical climates seem to be another exception. In the tropics, scarlet fever is very rare. In the Belgian Congo, Van Slype (1935) found more than 90 per cent. of 201 individuals to be Dick negative. In this connection, a curious phenomenon has been observed in ships passing from temperate to tropical latitudes and vice versa. Outbreaks of streptococcal infection, both on the outward and return journey, have included cases of scarlet fever while the ship was in the temperate but not in the tropical zone (de Langen, 1941). The functional condition of the skin itself seems to be a factor in insusceptibility in hot climates (see Dick test).

Race.—No race appears to be entirely exempt. Coloured races, whether yellow, red, brown or black, are affected less than the white (Schamberg and Kolmer, 1928).

Climate.—The disease is pre-eminently one of temperate climates. Its incidence has a definite gross relationship with latitude. Most cases occur in Lat. 30°–60° N. and 10°–40° S.

Season.—In England it is most prevalent from September to December, with a peak incidence in November. There is not infrequently a smaller flare-up in March or April. The correlation is with the opening of schools, rather than with the prevalence of the common respiratory diseases. In U.S.A. the disease prevails most in late winter and early spring (Schamberg and Kolmer). It is, however, an endemic disease and occurs all the year round.

Urbanization.—Large cities and populous areas are more affected than rural districts. In the former, epidemics tend to recur at intervals of about seven years. Epidemics of scarlet fever are practically always associated with an increased prevalence of other forms of hæmolytic streptococcal infection, *e.g.* tonsillitis, otitis media, sinusitis, erysipelas, puerperal and rheumatic fever.

Age.—The main incidence is in children, particularly the age-group three to ten years. This is probably associated with aggregation in schools and public places. Adolescents and young adults are next most frequently attacked. The disease is much rarer after 35 years but no age is exempt. It is practically unknown under six months and rare from

six to eight months. This applies alike to breast-fed and artificially-fed infants and to the infants of Dick-positive and Dick-negative mothers.

Sex.—There is no correlation with sex.

Clinical severity.—The prevailing clinical form in Europe and America, with certain exceptions, *e.g.* Roumania, is mild. The disease has become progressively milder during the last 60 or 70 years and particularly in the last 15 to 20 years. Mortality in England and Wales in the three years 1947–9 fell as low as 0·05 per cent. of notified cases (Min. of Health Rep., 1950). It should not be assumed that the present mild phase of scarlet fever will be permanent. Since Sydenham's description of the disease in 1675 there have been at least four alternate waves of mildness and severity in Britain. It is unknown whether these variations are associated with the prevalence of certain types of hæmolytic streptococci. In Roumania, very severe scarlet fever with mortality as high as 20 per cent. has been shown to exist at the same time as mild scarlet fever in a neighbouring district; the severe form there was shown to be associated with hæmolytic streptococcus of Griffith type 10 (Schwentker *et al.*, 1943).

Transmission.—Case to case or carrier to case infection by direct contact is probably the most common method. Children under five years are responsible for about eleven times as many secondary cases as are patients of fifteen years and over (Gordon, 1942). But the source of infection is sometimes a carrier or case of hæmolytic streptococcal infection other than scarlet fever. The infection may be conveyed by droplets, dust, manual transference or other route. Infectivity is greatest in the acute stage but may persist into the convalescent period. Some convalescents remain carriers for prolonged periods. Heavy nasal carriers are more dangerous than throat carriers (Hamburger *et al.*, 1945). Abrasions about the mouth and nares and purulent and other discharges in convalescents are apt to be infective. Fomites, *e.g.* pencils, toys, books; the blankets used by an acute case; the fluff and fibres of blankets suspended in the air of a ward or sick room or mingled with its dust (Cruickshank, 1940); the air and dust in the neighbourhood of a patient—all these can be heavily loaded with hæmolytic streptococci and are potent sources of infection. On the other hand, the dry, desquamated particles of epidermis formerly believed to be the main source of infection contain relatively few hæmolytic streptococci and are generally harmless unless they are contaminated with discharges.

Milk as a vehicle of infection is usually associated with explosive outbreaks but this is not an invariable rule. In most instances the original source can be proved to be human, contamination having occurred during the handling of the milk or having been transmitted to an abrasion on the cow's udder during milking.

Bacteriology.—In 1885, Klein isolated a streptococcus from the udders of cows whose milk was suspected of conveying the infection of scarlet fever. From that time until the Dicks' discovery of streptococcal exotoxin in 1924 many observations showed that the hæmolytic streptococcus was closely associated with scarlet fever.

In 1921 the Dicks swabbed the throats of volunteers with cultures of hæmolytic streptococci isolated from scarlet fever patients but failed to reproduce the disease, although a few developed tonsillitis. In 1923 the Dicks made a successful transmission of scarlet fever in a volunteer whose throat was swabbed with a culture of hæmolytic streptococci isolated from the septic finger of a nurse ill with surgical scarlatina. Another volunteer swabbed with the same culture developed tonsillitis and in three others no effect was produced.

The toxin of scarlet fever.—The key to this puzzle was supplied by the Dicks in 1924 when they investigated the toxic properties of filtrates of broth cultures of scarlatinal strains of hæmolytic streptococci and so discovered the soluble exotoxin, later called the erythrogenic or Dick toxin. An intra-dermal injection of 0·1 c.cm. of 1 in 1,000 dilution of such a filtrate gave rise to a circumscribed area of erythema in a certain proportion of individuals who had never had scarlet fever. (This became the basis of the Dick test.) The injection of larger doses occasionally gave rise to general symptoms of scarlet fever. Horses injected with such filtrates produced an antitoxin capable of neutralizing the toxic action of the filtrates. About the same time, Dochez (1924) produced an antiserum by injecting an agar culture of hæmolytic streptococcus subcutaneously in a horse. That Dochez' serum had antitoxic properties was shown by Blake *et al.* (1924) who produced with it a blanching or rash extinction test (Schultz-Charlton phenomenon), and also obtained a beneficial effects by its use in the treatment of early cases of scarlet fever. In the absence of any positive evidence in support of the virus theory, the foregoing is considered sufficient to establish a hæmolytic streptococcus ætiology of scarlet fever.

The next point was to determine whether there was a specific "*streptococcus scarlatinæ.*" The Dicks (1929) failed to obtain cross neutralization between erysipelas toxin and scarlatinal antitoxin and vice versa, and from this and other considerations, held that *str. scarlatinæ* and *str. erysipelatis* were immunologically distinct and separate organisms. Abundant experimental evidence has been accumulated to refute this claim. All of it favours the conclusion that the production of erythrogenic toxin capable of eliciting an erythematous skin reaction in man and which is neutralized by either scarlet fever convalescent serum or horse antitoxin, is a property of hæmolytic streptococci of human origin in general. Whilst different strains vary in the *amount* of toxin produced, *and some produce very little toxin*, practically all human pathogenic strains are capable of producing the same toxin, and, consequently, there is no specific and distinct *str. scarlatina* or *str. erysipelatis.*

Dick toxin could, theoretically, therefore be made from any of the human pathogenic strains. In practice it is usually made from type 10 or Dochez N.Y.5 strain as a basis, because this is a profuse toxin former. The toxin of predominant local strains are often added, *e.g.* that of types 1, 2, 3 and 4, in Britain. Methods of standardization both of toxin and antitoxin have, however, not yet been perfected, and a small percentage of anomalies may be met with in practice.

A complexity in the use of Dick toxin is the possible presence of bacterial constituents in the filtrate other than toxin. Ando *et al.* (1930) showed that crude filtrates might contain nucleo-protein which is heat stable, has no combining power with antitoxin, and produces local and general reactions in adults of sensitivity type. With inadequately prepared materials this second fraction could produce a pseudo-reaction. This would necessitate the use, with such material, of a control which has been autoclaved for one hour at 120° C. to destroy the relatively heat-resistant nucleo-protein. It is to be noted that the pseudo-Dick reaction is smaller and less intense than a true Dick reaction and *fades more slowly* —a time relationship which is the reverse of that in the Schick test. *With well prepared material, however, of a known standard a control test especially in primary Dick-testing of children is unnecessary.* As many as 800 Dick tests in children and young adults were done by Laurent (1943) with British made toxins and control without a single pseudo reaction (see also p. 1692).

The possible presence of bacterial (sensitivity) antigens or of over-diluted and too weak toxin in the Dick test material should be borne in mind in the event of anomalies occurring in connection with the Dick test. The test has been found, on the whole, to be reliable in practice and a sensitive measure of susceptibility or resistance to clinically recognizable scarlet fever. This is equally true in regions where the prevailing infection is highly toxic and in those where it is mild (Gordon, 1942). A negative test does not, of course, indicate immunity to hæmolytic streptococcal infection of other kinds than scarlet fever. There is now practically no doubt that all the clinical manifestations of scarlet fever, except the septic complications, are due to the soluble toxin produced in the local lesion and absorbed into the circulation in much the same manner as in diphtheria. Trask and Blake (1942), indeed, by means of Dick tests and Schultz-Charlton reaction (p. 1692), demonstrated the toxin in the blood and urine of scarlet fever patients in the acute stage, as well as the disappearance of the toxin after the injection of a large amount of antitoxin.

The hæmolytic streptococci of scarlet fever.—The two modern methods of classification of hæmolytic streptococci are by groups (Lancefield, 1933) and types (Griffith, 1926; Swift *et al.*, 1943).

Lancefield group A strains have all a common carbohydrate antigen C, which can be identified by means of a simple precipitin test. This group contains 26 of the 30 Griffith types of human pathogenic hæmolytic streptococci. The determination of a given strain as belonging to group A is presumptive evidence of it being a human pathogen. Other Lancefield groups which are now known to contain human pathogenic hæmolytic streptococci are groups B, C and G. Group B contains bovine mastitis strains which occasionally cause low-grade puerperal infections in women (Allison, 1942). Group C contains the Griffith types 7, 20, and 21 and group G the Griffith type 16 (Platou, 1941). These are known to cause tonsillitis, erysipelas and puerperal infections, and have also been identified with scarlet fever. F. Griffith (1926, 1927, 1935) showed by serological methods of agglutination and absorption that strains, isolated from scarlet fever, tonsillitis, erysipelas, puerperal fever, impetigo and other hæmolytic streptococcal infections can be classified into some 30 well-defined types. No one type is exclusively associated

with a typical clinical syndrome. In the early investigations (Glover and Griffith, 1931), types 1, 2, 3, and 4 were found in about 70 per cent. of scarlet fever cases in London. By 1936 this figure had changed to just upwards of 50 per cent. Other types which have been found to be associated with scarlet fever in London are types 6, 8, 10, 11, 12, 23 and 25 (Griffith, 1926, 1927, 1935); in Melbourne (Australia) types 2 and 17 have been commonly found. The Griffith type method of identifying individual strains has been of great value in epidemiology, enabling the sources and paths of infection to be traced. By means of it, Allison and Brown (1937) showed that the so-called "late septic complications" of scarlet fever, including relapses occurring in open wards, are practically always ward re-infections with hæmolytic streptococcus of a different type from that present on admission in a given case.

More recently Lancefield and her co-workers have typed hæmolytic streptococci by means of a precipitin technique for M substance and have raised the known number of types to more than 40. The important M antigen has thus been identified as the type-specific substance and it is also closely associated with the *virulence* of the strain. The development of M antibody for any particular type is associated with specific anti-bacterial immunity to the type.

Anti-bacterial immunity.—The Dick test measures antitoxic immunity, and scarlet fever, rarely, if ever, occurs in persons found to be Dick negative after reliable testing. Dick-positive persons do not, however, necessarily contract scarlet fever when infected with an epidemic scarlatinal strain. Indeed, in Roumania it was noted that 44 per cent. of such persons failed to develop any clinical illness (Schwentker *et al.*, 1943). In order to explain such phenomena (features also of diphtheria and other infections) anti-bacterial immunity is postulated. This is both *non-specific*—the defence barrier of mucus, cilia and phagocytes situated in the mucous membrane—and *specific*, namely M antibody. Indeed, we now know that in hæmolytic streptococcal infections, bacterial immunity is *type-specific*. This provides a theoretical explanation for the commonly observed relapses and re-infections with streptococci of a different type referred to above. This type-specific anti-bacterial immunity is quite independent of antitoxic immunity which protects only from the rash and toxæmia of scarlet fever.

Symptomatology

The usual incubation period is three days. It is always less than a week, but may be as long as six days or as short as twelve hours.

The onset is usually sudden and is accompanied by chilliness, vomiting, headache and a sore throat. In the average case the patient vomits only once or twice. Persistent vomiting in a child who is not liable to "acidosis" indicates a severe attack. A child often makes no complaint of sore throat. *In all acute fevers the throat should be examined as a routine.* The face is flushed and the skin feels hot and dry. The temperature, except in mild attacks, rises to 101° to 104° F. in a few hours. In children a rapid pulse-rate out of proportion to the height of the temperature is one of the features of the disease.

Fauces.—A band of fiery redness and infiltration extends across the fauces, soft palate and uvula. The swollen tonsils may protrude forwards making it difficult to see the follicular or patchy pultaceous deposit on

their opposing surfaces. As the rash develops, a red mottling appears on the palate and sometimes on the buccal mucous membrane (enanthem). The tonsillar exudate occasionally coalesces into a large patch and may be mistaken for diphtheria membrane. It is usually soft and wipes off, partially at least, without bleeding. A throat swab may even show morphological *C. diphtheriæ*. If the Schick test is negative this would merely denote the diphtheritic carrier state concurrent with the acute streptococcal lesion. Concurrent diphtheria and scarlet fever in the acute stage of both cannot altogether be excluded, but it is a very rare combination. In extra-faucial or surgical scarlet fever, the tonsils show no deposit and there is only moderate faucial congestion.

The *rash* appears in twenty-four to forty-eight hours. Occasionally it arises simultaneously with the first symptoms or may be delayed until the fifth or sixth day of illness, especially when there is concurrent upper respiratory infection of a different kind, *e.g.* influenza or coryza. The rash is composed of two elements, a number of closely set minute points, usually of a brilliant red colour, upon a diffuse somewhat paler uniform erythema. The tint varies from light pink to dark crimson, rashes with the more vivid colours persisting the longest. The individual punctate spots almost touch and rarely exceed half the diameter of a pin-head; in children with coarse skins they may be palpable, especially on the outer side of the extremities. The sides of the fingers often show a number of minute discrete colourless nodules which appear to represent the rash in this situation. The relative prominence of the component parts of the rash vary considerably; sometimes the uniform erythema is absent, more seldom the rash may lack its punctate feature on the limbs. Pressure will produce blanching of the rash, but often minute petechiæ are left, especially about the root of the neck and in front of the elbows where they form linear markings (*Pastia's sign*). When the rash is intense the skin may feel swollen, and minute yellowish white vesicles may appear (*scarlatina miliaris*). The site of first appearance of the rash is usually the root of the neck and upper chest whence it rapidly spreads to the rest of the trunk and limbs, although frequently it appears to be uniformly distributed at the outset. The palms and soles, scalp and face almost invariably escape the rash. The face, however, is characteristic. The cheeks are flushed and there is a well-marked zone of pallor around the mouth and nostrils (circum-oral pallor). The duration of the rash is variable. It may be present from a few hours to a week or more, although the usual duration is three days. The intensity and duration of the rash offer no certain indication of the severity of the disease. Severe cases of simple scarlet fever have usually a vivid prolonged eruption; in septic scarlet fever it is often blotchy, atypical and may be evanescent; in toxic scarlet fever dusky and ill-marked because of the peripheral circulatory collapse. A profuse rash will cause considerable itching.

The *tongue* in most cases becomes quickly covered with thick white fur, through which the swollen papillæ protrude as red points about the second day of disease (white strawberry tongue). The fur separates in patches or longitudinal streaks about the third day (peeling strawberry

tongue); and on the fourth day, it is completely denuded of fur, very red and raw with large papillæ (red strawberry tongue). The temperature remains high as long as the rash is vivid. Defervescence takes place, *pari passu* with the disappearance of the rash, the temperature falling by lysis to normal about the fourth to seventh day of disease, and all other symptoms subsiding at the same time in uncomplicated cases.

The *blood picture* in the acute stage shows a well-marked polymorphonuclear leucocytosis. Eosinophils tend to be normal or subnormal at outset, to increase steadily for a week or two up to about 10 per cent. and then decline to normal. A delayed increase may be associated with severe attacks and failure to decline normally suggests some complication. Absence of eosinophilia does not necessarily mean a bad prognosis.

Desquamation.—This usually sets in towards the end of the first week, but in brilliant rashes it may begin with the rash still present. The process usually starts about the root of the neck and upper part of the chest, or over the pubes, and spreads over trunk and limbs to the palms and soles where desquamation may be grossly flaky from the third to the fifth week or longer. Typically the first stage is the appearance over the papillæ of small white discs of dead epidermis, which separate, leaving small holes surrounded with a ring of raised epidermis (pin-hole desquamation). These rings spread and coalesce giving rise to branny and flaky desquamation. Occasionally after an intense and prolonged rash, the epidermis of feet and hands may be shed like a glove, leaving the skin red and somewhat tender but not raw or bleeding. Desquamation in young children may be of the branny rather than the pin-hole type. Little tags of skin are common around the root of the nails: these are apt to lead to infection of the nail bed, prolonging the period of infectivity. Peeling is, as a rule, proportionate to the intensity and duration of the rash, although it is sometimes entirely absent even after a good rash. Infants under one year rarely desquamate. As in other fevers where the attack is severe the hair may fall out to a considerable extent, but it is soon restored as the patient's health improves.

Clinical varieties of scarlet fever

A broad distinction should be drawn between (1) *faucial scarlet fever* in which the causal hæmolytic streptococcus is growing in tonsils and fauces and (2) *extra-faucial scarlet fever* in which the syndrome is secondary to hæmolytic streptococcal infection of some focus elsewhere, *e.g.* wounds, burns (surgical scarlet fever), genital passages (puerperal scarlet fever) or infected chickenpox vesicles. The latter will be considered first.

Extra-faucial scarlet fever.—The clinical characteristics are (1) mild faucial congestion only, without deposit on the tonsils, (2) a coated or papillated tongue, (3) a rash which may be mainly aggregated in the neighbourhood of the focus, *e.g.* the abdomen and flanks in puerperal cases, or may be normally distributed. Since there is no hæmolytic streptococcal lesion in the fauces the condition is not infective by droplet infection but may be, of course, by manual transference from the primary

streptococcal lesion. Surgical scarlet fever following the operations of tonsillectomy and for cleft palate is not uncommon and cannot be readily distinguished from primary faucial scarlet fever. Prophylactic sulphonamide or penicillin therapy is recommended for a few days after these operations, especially where the patients are nursed in open wards and so are exposed to extraneous hæmolytic streptococcal infection.

Faucial scarlet fever.—This includes three main varieties : (1) *simple scarlet fever*, the symptoms and course of which have been described above, (2) *septic or anginose scarlet fever* and (3) *toxic or malignant scarlet fever.*

Simple scarlet fever.—This is by far the most common form. The acute stage is as described above or much milder. Symptoms and rash are sometimes so trivial as to escape detection in the acute stage, and the real condition may be undiagnosed or recognized only with the onset of desquamation or nephritis. "*Scarlatina sine eruptione*" is an old term for cases with tonsillitis which do not exhibit a rash but which appear to have been infected from a scarlet fever source. Such cases generally occur in persons who are immune to scarlet fever (Dick-negative reactors) and the condition would be classified to-day as streptococcal tonsillitis.

Septic or anginose scarlet fever.—In this form the hæmolytic streptococcus deeply invades the tissues of the tonsils, fauces and pharynx producing extensive ulceration and œdema which cause extreme pain. Swallowing becomes difficult owing to the pain ; breathing becomes obstructed and noisy owing to the swelling of the tonsils, which indeed often rub against one another, increasing the ulceration. The ulcerated surfaces become covered with soft yellowish grey exudate or muco-pus, and as this stage is usually reached after the rash has faded, the condition bears a superficial resemblance to toxic diphtheria. It is distinguished from it by the pain and tenderness and the absence of adherent membrane. Profuse muco-purulent nasal discharge excoriates the nostrils and upper lip. A collar of enlarged submaxillary glands soon develops and, in the worst cases, there is inflammatory œdema, cellulitis and even gangrene of the surrounding skin. Nevertheless, in most cases, this great swelling of the neck can be readily distinguished from the "bull-neck" of diphtheria by its tenderness and lumpy character, individual glands being usually palpable. The cervical glands tend to suppurate. Suppurative otitis media develops within a few days in most cases. The temperature remains high and the patient, usually a young child, is restless and may be delirious. Local sloughing may occur in fauces, pharynx or neck and, rarely, this may lead to uncontrollable secondary hæmorrhage. Broncho-pneumonia may develop in the second or third week. The rash is often ill-marked and atypical. It may take the form of a patchy erythema, chiefly seen on the limbs, or may be accompanied by a secondary allergic blotchy or circinate erythema. In young children under three years, septic scarlet fever was highly fatal in the past, usually from local sepsis, septicæmia, exhaustion, or broncho-pneumonia in the second or third week. Recovered cases often ran a stormy course for three or four weeks before the temperature fell. Septic scarlet fever as here described is now a preventable disease. Its development can be stopped by timely use of

sulphonamides or penicillin especially when combined with streptococcus antitoxin.

Toxic or malignant scarlet fever.—In this form, which is usually fatal and fortunately rare, there is profound toxæmia with prostration but little or no bacterial invasion in the fauces or pharynx. Severe vomiting at onset may be followed by convulsions, delirium, stupor or coma. There is high temperature, marked tachycardia, poor pulse and low blood pressure. The cardiac failure and the peripheral circulatory collapse cause the rash to be ill-developed, dusky or cyanotic. For this reason the rash is frequently missed, and the nervous symptoms, delirium or coma may suggest a diagnosis of cerebro-spinal fever. There are, however, no sign of meningeal irritation. The punctate rash, although ill-developed, can be brought out by the application of heat. The tongue usually shows enlarged papillæ. The mild degree of faucial injection in such a severe illness is apt to be misleading. This form is usually fatal within a few days. The only hope of saving the patient lies in early accurate diagnosis and efficient specific treatment—a good concentrated streptococcus antitoxin in large intravenous doses, *e.g.* 30,000 to 90,000 units combined with sulphonamides, penicillin, aureomycin or chloromycetin. A very rare variant of toxic scarlet fever is the hæmorrhagic form, in which, in addition to the profound prostration, petechial and purpuric hæmorrhages appear in the skin and mucous membrane soon after onset.

Intermediate forms between simple and septic scarlet fever are of relatively common occurrence. Mixed toxic and septic forms are also occasionally seen.

Complications and their Treatment

Since scarlet fever is both a septic and a toxic disease, its complications can broadly be divided into septic and toxic groups.

Early septic complications.—The most common and probably the most important is *acute suppurative otitis media.* The incidence of this complication varies directly with age and type of disease whether simple or septic. It is particularly prevalent before the age of five years, and at this age few with the septic type of scarlet fever escape suppurative otitis media. Amongst " mild " as distinct from " septic " cases treated by Goodall in the Eastern Hospital 1895–1914 (10,700 cases) the incidence at 0 to 5 years was 13·73 per cent. ; at 5 to 15 years 5·15 per cent. ; and at 15+ years 2·63 per cent. At all ages the incidence of otitis media in " mild " cases was 7·56 per cent. and in mild and septic cases taken together was 11·3 per cent. (Goodall *et al.* 1929). A considerable reduction in such figures has been effected in more recent years, partly owing to the decline in severity of scarlet fever, and partly owing to the control of the disease by antitoxin, chemotherapy and antibiotics. Even with a good antitoxin in the pre-sulphonamide era it was possible to control the incidence of otitis media partially. Thus, in the Park Hospital, 1933–5, amongst 3,161 cases treated with intravenous or intraperitoneal antitoxin combined with a short isolation period, the incidence was 0 to 5 years 3·9 per cent. ;

5 to 10 years 1·9 per cent.; 10+ years 0·5 per cent. (Banks, 1936). Such figures were, however, exceptional. Even now in a mixed series of all ages treated without penicillin an incidence of 8 per cent. is not uncommon, this figure including both early and late otitis media. The first sign of otitis media observed in young children is not infrequently the appearance of purulent discharge at the external auditory meatus. There may be mild pyrexia preceding it but seldom any complaint of pain. Myringotomy is thus not usually applicable in young children. Moreover, where I have seen it applied, I concur with Layton's opinion (1930) that it has little if any effect on the course of the disease. A most effective treatment of acute otitis media to-day in reasonably healthy children is early, efficient and sustained chemotherapy. The fear of chemotherapy producing partial superficial healing and latent mastoiditis is one which need only be associated with late or timid dosage or wrong choice of drug. For many cases, sulphathiazole in adequate four-hourly dosage is sufficient. Its use should preferably be controlled by bacteriological examination of a swab from the ear-drum for sulphonamide-resistant organisms. If sulphonamide-resistant hæmolytic streptococci are found, or if striking resolution is not evident on otoscopic examination within three or four days, penicillin, aureomycin or chloramphenicol should be immediately substituted. High dosage, as for severe infections, is necessary for acute otitis media. Not less than 3 gm. sulphathiazole daily should be given at ages 0 to 3 years; 4½ gm. daily at ages 3 to 10 years, and 6 gm. daily at ages 10 to 15 years. Penicillin dosage should be not less than 100,000 units four-hourly intra-muscularly. Chemotherapy should be continued for at least three days after the membrana tympani is seen to be quite dry on otoscopic examination. Such chemotherapy, applied within three or four days of onset, results in a dry healed tympanic membrane in most cases within a week or ten days. Mastoid operations are practically abolished. Among 2,434 cases of scarlet fever and measles in Park Hospital during the years 1940–43, when sulphathiazole only was used for otitis media, only four mastoid operations were required compared with nineteen among 1,525 cases in the year 1938. Since penicillin became available for the sulphathiazole-resistant cases, the average period of healing has been considerably speeded up and the mastoid operation practically eliminated.

Other local extensions of the infection from the fauces, *e.g. submaxillary adenitis*, *stomatitis*, *rhinitis*, *sinusitis*, *dacryocystitis*, *retro-pharyngeal abscess*, *cellulitis*, (*e.g.* orbital Ludwig's angina), *facial erysipelas*, *laryngitis*, *bronchitis*, and *broncho-pneumonia* need only be mentioned here. Tonsils and adenoids are sometimes enlarged for months after scarlet fever. Associated sinusitis should be looked for by X-ray if necessary. There should be no haste to operate; the child should be taught to blow the nose. A sign suggestive of *ethmoiditis* is a well-marked swelling of upper and lower eyelids, usually combined with nasal obstruction. Post-pharyngeal abscess causes pain and difficulty in swallowing; the bulging posterior pharyngeal wall can be seen or felt with the finger. Like peri-tonsillar abscess it can usually be successfully treated by penicillin

alone. If incision is ever necessary this should not be done until the abscess is mature and pointing. The scalpel should have the point guarded with adhesive strapping $\frac{1}{8}$ inch from the end. After incision the child's head should be instantly turned to the side and lowered in order that pus may not be inhaled into the trachea.

Septicæmia and pyæmia may occur in the severer cases of simple scarlet fever, but are more common in the septic type. They may appear early, from the original infection, or late from re-infection. The most common pyæmic manifestation is purulent arthritis, usually in the knee or other large joint. Purulent pericarditis or peritonitis may occur. Streptococcal meningitis is usually secondary to mastoid disease. In primary streptococcal peritonitis in which there is no evidence of acute appendicitis or other local focus laparotomy will rarely be necessary. Penicillin or a newer antibiotic in adequate dosage should be sufficient. Up to 1936, the fatality rate was 70 per cent.

In 1938, a boy aged eight years was successfully treated for this complication in the Park Hospital, by means of sulphapyridine and without laparotomy. Blood culture and paracentesis abdomini before chemotherapy yielded hæmolytic streptococcus type 4. During the succeeding six days large amounts of thin purulent peritoneal fluid were aspirated off but from this fluid no growth was obtained (Banks, 1939).

Late septic complications.—These occur after the subsidence of the acute stage, generally after the first two weeks. It is now generally accepted that they are chiefly caused by re-infection with hæmolytic streptococci of different types from that causing the original infection. Where patients are detained in multiple-bed wards for long periods 50 to 70 per cent. of them may be so re-infected; the majority of these, however, have latent or sub-clinical infection, and only a minority show clinical manifestations. *Relapse* of scarlet fever which rarely occurs before the fourth or fifth week is invariably due to such extraneous infection. The commonest late septic complications are *secondary tonsillitis*, *secondary adenitis*, *late suppurative otitis media*, *purulent rhinitis* and various forms of skin sepsis, particularly *impetigo* and *paronychia*. The best prophylactic for late septic complications is early discharge from hospital. The isolation period in hospital should not, unless for special reasons, extend beyond two to three weeks. Experience of some 18,000 cases of scarlet fever since 1927 shows that this is quite a practical policy, even when dealing with a severe type of scarlet fever. Adequate use of antitoxin, and, if necessary, chemotherapy in the acute stage make it unnecessary to detain uncomplicated cases in hospital or in isolation at home longer than about two weeks. Arrangements should, however, be made for examination of urine up to the twenty-fourth day of disease. The writer agrees with Rolleston and Ronaldson (1940) that nephritis is exceedingly rare in cases well treated with a good antitoxin.

Toxic-allergic complications.—(*a*) Direct toxic complications occur usually in the first week. The early tachycardia of simple scarlet fever, the toxic myocarditis of the malignant variety, and the relatively common functional soft systolic heart murmurs, as well as the albuminuria of the

first few days of the disease (acute focal nephritis) are likely to be the result of direct toxic action on the heart, kidneys, etc. (*b*) The most important complications in this group, nephritis and acute rheumatism, are probably caused indirectly by toxic action evolving some form of allergic mechanism. They both tend to occur after the acute stage of the disease has passed, nephritis in the third or fourth week, and rheumatism rather earlier, from the end of the first to the third week.

NEPHRITIS.—Scarlet fever is one of the commonest causes of nephritis in children. Not infrequently the onset of hæmaturia combined with some desquamation of the skin and a history of sore throat two weeks or so previously points to a missed attack of scarlet fever. It usually arises between the eighteenth and twenty-third day of the disease (although there is a form of acute focal nephritis which arises soon after onset). The onset may be insidious with the discovery of albuminuria on routine examination followed by smoky or red urine. More commonly there is mild fever, headache, vomiting, and puffy pallor of the face; there may be also concurrent enlargement of cervical glands, secondary tonsillitis or otitis media. Except for the puffiness of the face, there is little œdema in most cases but generalized dropsy occasionally supervenes especially where the nephritis is untreated in the acute stage. The blood pressure is nearly always raised and blood urea may be normal or increased up to 80 mgm. or more per 100 c.cm. Retinal changes are uncommon. Convulsions, which if generalized may be followed by coma, sometimes occur within a few days of onset of the nephritis. This condition was formerly attributed to uræmia, but as it often occurs in cases with normal blood urea and marked hypertension, it is now described as hypertensive encephalopathy. It is probably ischæmic in nature due to spasm of the cerebral arterioles. The prognosis in scarlatinal nephritis, as in most type I (post-infective, glomerular) nephritis is good, when it is appropriately treated, the condition usually clearing up within seven weeks or less. A small proportion of cases, however, progress to general anasarca and may be intractable. The albumin-globulin ratio in the blood becomes diminished, heavy albuminuria persists, the condition assumes partly the character of a type II nephritis (nephrosis) (Ellis, 1942) and is commonly fatal within two or three months; or it may clear for a time with the probability of becoming subacute or chronic. The incidence of nephritis, which at the beginning of the century was from 4 to 7 per cent., has undergone a progressive decline in Britain. Osman (1934) reported an incidence of 1·74 per cent. among 10,000 cases of scarlet fever in London but since then it has greatly declined. Although nephritis is liable to occur after mild as well as severe attacks of scarlet fever, it is very rare amongst cases treated adequately with antitoxin in the acute stage. Thus in 1936, Ronaldson had no instance of nephritis among 674 cases treated with large intramuscular doses of antitoxin, and Banks (1936) had an incidence of 0·2 per cent. amongst 3,161 cases treated with intravenous or intraperitoneal antitoxin in three years 1933–5 (one-seventh of the incidence amongst controls not treated with antitoxin). Similarly in Hoyne's

antitoxin-treated series (1935) the incidence was one-sixth of that of the controls.

Rheumatism and carditis.—The relation of juvenile acute rheumatism to preceding and recurrent attacks of upper respiratory streptococcal infection has been increasingly emphasized in recent years. Chemoprophylaxis of these infections by prolonged administration of sulphanilamide throughout winter and spring to rheumatic children has been successful not only in preventing streptococcal infections but also in saving the children from further rheumatic episodes (Kuttner and Reyersbach, 1943). Scarlatinal rheumatism is in no way different from that which occurs after tonsillitis or other streptococcal infection. It rarely occurs below the age of six years. A tender serous arthritis is the most common manifestation, but the muscles, fasciæ and tendons may also be affected. Subcutaneous nodes can sometimes be palpated. The incidence of serous arthritis after scarlet fever was commonly about 4 per cent. in the pre-antitoxin era, but has since diminished, especially in cases well treated with antitoxin. In my series of 3,161 cases treated with intravenous or intraperitoneal antitoxin in 1933–5, the incidence of rheumatism was 0·5 per cent., and that of carditis was 0·06 per cent. The carditis of scarlet fever is similar to that of rheumatic fever following acute tonsillitis ; it does not appear before the thirteenth day of disease. Its incidence has also considerably diminished during the present century. In 1900–14 endocarditis in the M.A.B. Hospitals, London, had an incidence of 0·32 to 0·92 per cent., but E. H. Place (1932) at Boston found less than 0·1 per cent. Endocarditis occasionally arises insidiously unpreceded by manifest rheumatic symptoms.

Symptomatic purpura.—This is a rare complication, probably allergic in nature, about which little is known. It occurs in convalescence, from the second to the fifth week. In a child who seems relatively well, purpuric hæmorrhages suddenly appear in skin and mucous membranes ; there may be large ecchymoses in the subcutaneous tissues and even hæmaturia and melæna. The spleen is not usually enlarged. There appear to be at least two types of purpura. The first and most common is associated with a strongly positive capillary fragility test, with or without thrombocytopenia, and with coagulation and prothrombin time normal. The lesion here appears to be in the capillary endothelium and possibly in the bone-marrow as well. In the other type the blood picture including the platelet count is not far from normal, but the coagulation time is grossly increased, and prothrombin and even fibrinogen deficiency is marked. This type suggests liver dysfunction probably due to toxic action. In a recent case of the latter type in a boy of eight years under my care, a marked prothrombin and fibrinogen deficiency associated with purpura cleared up in about ten days, and then, ten days later, double femoral thrombosis occurred—a most unexpected switch-over. Both mild and severe cases of purpura occur and neither seem to be related to the severity of the primary disease. It seems probable that genetic factors are principally involved, especially an innate high degree of susceptibility to capillary damage and sometimes also to thrombocytopenia.

A similar mechanism probably operates in purpura following rubella (Ackroyd, 1949). Of the five cases seen by me, two were rapidly fatal. Treatment is by vitamin C (*e.g.* 500 to 1,200 mgm. ascorbic acid daily) when there is capillary fragility, and by vitamin K when there is prothrombin deficiency. In severe cases blood transfusion is required.

POST-SCARLATINAL DIPHTHERIA.—Diphtheria, usually of the mild anterior nasal type, was formerly called the "bugbear of scarlet fever wards." With modern treatment it is uncommon, partly because a dose of streptococcus antitoxin given for treatment usually contains a few hundred units of diphtheria antitoxin owing to basal diphtheria immunity in the horse, and partly because of the modern short period of isolation. Nevertheless, diphtheria should be suspected in any case showing blood-stained nasal discharge and sores about the nares and lips. In such a case, examination of the front part of the nasal septum for diphtheria membrane should on no account be omitted. Swabs should be taken of any suspicious exudate in nose or throat.

Second attacks.—Verified second attacks more than six weeks after the primary attack are less rare than formerly owing to the mildness of the disease. Many alleged second attacks are to be discounted because errors of diagnosis in scarlet fever are frequent. Second attacks are, however, quite possible in the small minority of cases which remain Dick-positive reactors after the primary attack.

Return cases.—These are cases which arise in the patient's home after he has been discharged from hospital. It is impossible to secure freedom from infection in every case released from isolation. Although there may be no apparent infective foci, *e.g.* nasal or ear discharges and abrasions about nose or mouth, there may be a heavy carrier infection. The carrier state is at its lowest about the end of the third week in hospital (Brown and Allison, 1935). Routine negative release swabs are unattainable and should not be sought. Desquamation is not infective. Cases showing clinical signs of streptococcal infection should be detained in isolation, but all others should be released as early as possible. A return case rate of two to three per cent. in large cities is not abnormal. For two weeks after return home all possible precautions to prevent infection should be taken.

Morbid anatomy

Post-mortem examination in the acute stage reveals the signs common to any acute infection. There is, however, marked lymphoid enlargement, with prominence of Peyer's patches and of the Malpighian bodies in the spleen. Occasionally focal necrosis of the liver has been found. The rash, unless petechial, disappears at death. The fauces in toxic cases show only tonsillar enlargement, and in septic cases ulceration and sloughing. In nephritis, various types and stages of kidney lesion have been described. Commonly *the glomeruli are ischæmic* from swelling of the capillary endothelium, and engorged afferent arterioles become narrow and thread-like just short of the glomeruli. Culture of the heart blood frequently reveals hæmolytic streptococci.

Diagnosis

Three special diagnostic procedures are available; *the Dick test*, *Schultz-Charlton test*, and *bacteriological* investigation.

Dick test (see also p. 1680). –This is a skin test of the immunity type like the Schick test. As originally described it consisted of the intradermal injection of 0·1 c.cm. of 1 in 1,000 dilution of the filtrate of a broth culture of a scarlatinal streptococcus (Dick toxin), and a control test in the other arm with similar material inactivated by boiling. Such material was soon found to be too variable for reliable results. As there was no satisfactory method of standardization of Dick toxin in animals the " skin test dose " was introduced. It is defined as the smallest amount of a toxic filtrate which, injected intradermally into the forearm, will produce in the *majority* of susceptible individuals an area of erythema not less than 1 cm. in diameter. This quantity is thus not fixed but variable to some extent. In recent years the intra-dermal test in rabbits has been much improved and is now used routinely to determine the " skin test dose." The material issued from British laboratories contains one skin test dose in 0·2 c.cm.—an amount more suitable for intradermal injection than 0·1 c.cm. Pseudo-reactions are almost unknown with primary Dick-testing in children, and for them at least a control test is unnecessary except for Dick-testing after immunization against scarlet fever. In the latter case a confusing sensitivity reaction is occasionally produced. The Dick reaction is a circumscribed area of erythema, usually without infiltration, and *it may be very faint*, so that it can only be seen on compressing the skin of the forearm. It appears in six to twelve hours and disappears rapidly after twenty-four hours, and is thus *a much more rapid reaction than that of the Schick test*. A positive reaction is a *fairly* reliable index of susceptibility to scarlet fever. But it must be emphasized that different preparations of Dick test toxin show some variation in potency, due to the difficulties of exact standardization. Anomalies in its action are therefore more frequent than in the Schick test. Infants under six months are usually Dick negative (see p. 1678). A graph showing the percentage of Dick-positive reactions according to age is appended (fig. 579).

In the acute stage of scarlet fever theoretically 100 per cent. should be positive. The test cannot, however, be applied in an area of skin occupied by a brilliant rash, and again it may become negative as early as the fifth day, although, more commonly, it remains positive for the first week or two. If the test is applied when the rash is beginning to fade, *e.g.* third or fourth day of the disease, and good reliable test material is used, it has been found positive in as many as 93 per cent. of cases of scarlet fever (Laurent, 1943). After scarlet fever 10 per cent. or more of cases remain Dick positive for several weeks, and it is amongst these that relapses may occur. Contrary to what is sometimes stated, mild cases *usually* become Dick negative quickly, often by the fourth or fifth day.

The Schultz-Charlton test.—This is a " blanching " or " rash extinction " sign produced by intradermal injection of 0·5 c.cm. of convalescent scarlet fever serum, or 0·2 c.cm. of a 1 in 10 or 1 in 100 dilution

of streptococcus antitoxin according to its potency. The injection is made in an area of bright red rash, usually in the skin of the abdomen. If the test is positive an area of blanching appears at any time up to fourteen hours and usually lasts for the duration of the rash. The test is of limited value in the diagnosis of scarlet fever. The absence of a positive reaction does not negative the diagnosis ; it is often unsatisfactory in coarsely punctate and other anomalous rashes and *its value diminishes with ageing of the rash* (Blake, 1927). It occasionally gives corroborative information in differential diagnosis between scarlet fever and rubella, scarlatiniform prodromal rashes or drug and serum rashes.

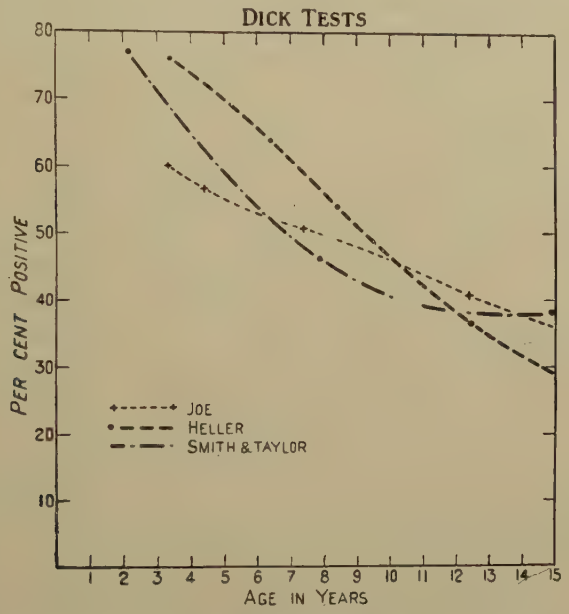

FIG. 579.—CURVES SHOWING THE PERCENTAGE OF DICK-POSITIVE REACTIONS ACCORDING TO AGE.

BACTERIOLOGICAL INVESTIGATION.—A throat swab plated out on blood agar invariably yields a profuse growth of hæmolytic streptococci in faucial but not in extra-faucial scarlet fever. In the latter the hæmolytic streptococcus is obtained from the infected wound, burn or other focus. The swab report is significant in diagnosis only when considered in conjunction with the clinical picture. It is an advantage in connection with possible subsequent developments to have the hæmolytic streptococcus typed, but this takes forty-eight hours or more. The *antistreptolysin titre* of the blood serum may be used in the second or third week of the disease to indicate recent hæmolytic streptococcal infection. Titres above 1 in 150 are considered significant.

Differential diagnosis.—Before the rash appears, or in cases with a faint or transient rash, the faucial inflammation may be confused with

follicular tonsillitis, quinsy, diphtheria, Vincent's angina, glandular fever, febrile catarrh, or pneumococcal pharyngitis (see diphtheria, p. 1713). Septic scarlet fever, seen about the fourth or fifth day after the rash has faded, is not infrequently mistaken for diphtheria. The pain and tenderness, the ulceration, the post-nasal purulent discharge, the papillated tongue and absence of false membrane all strongly suggest scarlet fever. Schick and Dick tests and throat cultures may be required to clear up the diagnosis. The *erythema* may be confused with drug rashes from belladonna, quinine, iodides, salicylates, chloral, sulphonamides or antibiotics and with enema, serum and allergic rashes. These all tend to be of non-uniform distribution and character (*e.g.* maculopapular or urticarial in some parts) to invade the face and extensor surfaces and to be unassociated with faucial angina. The scarlatiniform type of rubella (p. 1767) may be confusing, and here the post-cervical glandular enlargement, the Schultz-Charlton reaction, the Dick test and throat swabs are of great value. *Desquamation* is most commonly, but not by any means invariably, a late sign of scarlet fever. Faint rashes may produce no desquamation. Pin-hole desquamation, though very suggestive of scarlet fever, may occur after any punctate erythema, *e.g.* that produced by irritating applications or garments. Flaky desquamation on the hands in the third week and the feet a little later is very suggestive of scarlatina. In acute exfoliative dermatitis, the desquamation is severe and persistent and confusion unlikely to arise.

Prognosis

This varies enormously according to the type of scarlet fever and is also dependent to some extent on the treatment given. Fatality rates in this country are now extremely low, chiefly because of the mild type prevailing, but also because of specific treatment. Complications may bring about sequelæ of a chronic nature. Of these, chronic nephritis and carditis are now rare in this country. Chronic otorrhœa with deafness and its cerebral accompaniments is still the most frequent and formidable morbid condition resulting from scarlatina. Its prevention depends upon prompt and adequate chemotherapy (sulphathiazole or penicillin) in the first few days of the acute otitis (p. 1696) and upon improvement in the general health of the child population.

Treatment

This may be considered under the heads (*a*) antitoxin, (*b*) chemotherapy, (*c*) general and local measures, (*d*) prevention of re-infections.

(*a*) Antitoxin.—An important measure in the treatment, particularly of cases with bright rashes, is the injection of 10,000 to 20,000 units of a potent, enzyme-treated streptococcus antitoxin as soon as possible after the appearance of the rash. Such an antitoxin directly neutralizes the erythrogenic toxin and if injected within the first three days of disease produces three striking effects: (1) rapid reduction of toxæmia with

feeling of well-being in six to eighteen hours, according to the dose and route of injection, (2) similar rapid subsidence of local congestion and œdema in the fauces, and (3) fading of the rash in twelve to thirty-six hours. The effects are naturally less striking if the case is very mild or if the injection is made on the fourth or fifth day. After the fifth day antitoxin is generally useless except in septic cases in which faucial œdema is still present. In such cases, intravenous injection of an adequate dose (*e.g.* 30,000 units) has often a remarkable effect—the œdema is reduced, the swollen tonsils fall away from one another, the ulceration begins to heal, an airway and drainage are re-established, swallowing is less painful and the natural defence mechanism begins to operate effectively. It is often stated that antitoxin is useless in septic cases. This is so when an ineffective dose is given by the intramuscular route, but those who have used an adequate intravenous dose in such cases know its value. In toxic or malignant cases, a similar or larger intravenous dose is indicated at the earliest possible moment.

Streptococcus (and diphtheria) antitoxin, has been greatly improved since 1938 by the enzyme (pepsin) process of concentration. In this process the proteins of the serum are partially disaggregated, allergenically active protein is reduced to a trace, and the antitoxin is concentrated in much smaller bulk than with the old process of precipitation of proteins by ammonium sulphate. Enzyme-treated antitoxin can be injected intravenously without shock reaction in most cases and even the ordinary serum rash and sickness has an incidence of less than 5 per cent. with the best preparations. A dose of 9,000 U.S.A. units, formerly contained in about 30 c.cm., may now be concentrated in as little as 1 to 3 c.cm. A unit is defined in the U.S.A. as the amount of antitoxin which neutralizes fifty skin test doses of toxin. Some American antitoxin, however, is now measured in units, which neutralize one hundred skin test doses of toxin ; 2,000 or more units are contained in 1 c.cm. Since the skin test dose is a variable quantity, a unit of streptococcus antitoxin is an inexact measure. Hence it is desirable to give high dosage, *e.g.* 20,000 units, to cover possible variations in potency, provided that expense is not a paramount consideration. The intra-muscular route is the one most generally used, but it should not be forgotten that the intravenous route is more than twice as effective dose for dose, and that the intraperitoneal route comes next in efficiency (Park, 1921 ; Platou, 1923). The latter route might with advantage be more largely employed in infants and young children in whom intravenous technique is difficult. Local peritoneal reaction due to sensitivity to serum proteins is rare at this age and absorption from the peritoneum is rapid. Abdominal pain and tenderness due to local sensitivity reaction occasionally occur but pass off in a few hours. Intra-peritoneal injection should never be attempted unless rigid asepsis can be employed. The syringe and needle should always be heat sterilized. A single dose of antitoxin is nearly always sufficient for the treatment of scarlet fever. A second dose is hardly ever needed unless the first has been grossly underestimated.

The dangers of serum therapy with enzyme-treated antitoxin are slight but not absolutely negligible. Before injecting serum, inquiry should always be made for a history of asthma. Although it is only horse asthmatics who are markedly serum sensitive as a rule, it is wise to exclude all asthmatics from serum therapy if possible. If serum is essential in asthmatics, commence with a dose of 0·1 c.cm. of 1 in 100 dilution

subcutaneously and proceed with three to six gradually increasing doses subcutaneously or intramuscularly every half-hour before the full dose is given intramuscularly. In other allergic conditions, *e.g.* hay fever, urticaria and eczema, serum sensitivity is exceptional. Previous serum injections, including diphtheria immunization with toxoid-antitoxin floccules (T.A.F.), are apt to induce a state of sensitivity characterized by accelerated serum reaction (*e.g.* five days after re-injection of serum) or local œdema or rash at the site of injection. A general anaphylactic reaction in these cases, however, is very rare. Accordingly in these minor allergic conditions and in cases where serum has previously been given, it is generally sufficient to give one injection of 0·25 c.cm. subcutaneously in order to test for *general* sensitivity, and then wait two hours. If there is no general reaction in that time the full dose may be given. Intradermal and conjunctival sensitivity tests are unreliable as tests of general sensitivity both in a positive and negative sense and are not recommended. *Dermal* sensitivity does not necessarily or even commonly run parallel with *general* sensitivity. In children, test material in the conjunctiva is usually washed out by tears. A reaction is rare but if it occurs it may be dangerous to the eye. Anaphylactic shock cannot always be foreseen, but when it occurs, the fatal issue can in most cases be prevented by immediate treatment. A hypodermic syringe with an ampoule of adrenaline should always be ready for instant injection if any sign of shock appears. *Patients should always be warm when serum is injected and further warmth applied immediately if necessary.* If the shock takes a respiratory form an injection of lobeline chloride 3 mgm. to 10 mgm. is often effective. It is incumbent on those who inject serum to make preparations for the instant application of such measures should the necessity arise. A few minutes' delay may be fatal. The above procedure is recommended as a result of experience with serum in the British Isles. The problem appears to be rather more formidable in America. The argument that serum therapy is unwarranted in scarlet fever because serum sickness may prove worse than the disease has lost its force since the introduction of enzyme-treated antitoxin.

Convalescent serum has been employed in some parts of America in preference to antitoxin, partly because of its alleged antibacterial as well as antitoxic action and partly to avoid the risks of anaphylaxis. Its antitoxin content is very low, and dosage must therefore be as high as 50 to 100 c.cm. (Thalimer, 1938). With the use of human serum a risk which cannot altogether be disregarded is the conveyance of hepatitis (*Lancet*, 1943).

(*b*) Chemotherapy.—Any of the sulphonamide drugs or penicillin may be employed as a routine during the acute stage in addition to antitoxin. In septic scarlet fever this should always be done, but in simple scarlet fever it is the writer's practice to reserve them for any septic complication when full dosage is employed without delay. It should be realized that sulphanilamide, although formerly widely employed, is the weakest of the sulphonamides. Sulphathiazole and sulphadiazine are more potent and satisfactory drugs against the hæmolytic streptococcus although

sensitivity rashes, including erythema nodosum are now more common with sulphathiazole than formerly.

Penicillin treatment 100,000 to 200,000 units at twelve-hourly intervals for six days, without antitoxin, was advocated by Jersild (1948). The rash is not influenced by this treatment but streptococcal infection of the pharynx, including the carrier condition, is greatly reduced or obliterated and septic complications largely prevented. Some now give a depot dose of 300,000 units procaine penicillin once daily for six days. It is claimed, as for antitoxin treatment, that the stay in hospital can be reduced to eight to fourteen days by this measure. Appraisal of this method must await larger trials on severe cases. The prevailing mild scarlet fever is now usually treated with penicillin only.

(*c*) General and local measures.—The child should be confined to bed and given a fluid diet with glucose drinks for the first day or two. In serum-treated cases the temperature usually falls within twenty-four to forty-eight hours of the injection, and the urine is then free from albumin and acetone, and appetite and general condition improved. In such circumstances full nutrition should not be withheld. Specifically treated and mild cases may have light diet on the second day and full diet on the third day. Moreover, they are allowed up about the end of the first week. They should be kept reasonably warm. Contrary to what has been feared this routine has led to no increase of nephritis. It has, indeed, made for much more rapid convalescence than formerly and rendered uncomplicated cases quite ready for discharge from hospital after two to three weeks' isolation. It is desirable, however, to make arrangements for a urine test about the twenty-fourth day of disease.

In cases not responding so rapidly as the above, pyrexia over 102° F. should be treated by tepid sponging; restlessness and insomnia by chloral, Dover's powder or a barbiturate like somnifaine (Roche). If the cause of the pyrexia is not in the fauces, a complication, *e.g.* adenitis or otitis media, should be looked for and treated. Unless the fauces are badly ulcerated no local applications to the throat are necessary or desirable in children, but it is most important that the nursing toilet of the mouth and tongue and lips with cleansing alkaline lotion or compound glycerine of thymol and boric ointment be carried out as often as is required to make the patient comfortable.

(*d*) Prevention of re-infections—isolation period.—Most of the complications of scarlet fever treated in hospital are due to re-infections with extraneous hæmolytic streptococci. In an open ward skilled aseptic barrier nursing, scrupulous ward cleanliness, good ventilation and adequate bed-spacing are essential but even these fail to prevent a certain amount of infection passing directly from patient to patient or through the air or dust by inhalation. The best ultimate safeguard is a short isolation period of two or three weeks for uncomplicated cases, and no undue prolongation of in-patient treatment for complicated cases (p. 1686). Relapses of scarlet fever begin to appear amongst patients kept four or five weeks in hospital. Before discharge from isolation all cases should be clinically free from any acute form of inflammation in throat, nose, ears including tympanic

membranes, sinuses, glands and skin: the urine should be free from albumin, cardiac efficiency should be unimpaired, although occasionally functional murmurs may be present, and general nutrition, brightness and activity up to a good standard. This is quite attainable for the vast majority in the period stated (see also "return cases" p. 1691). After release from isolation children are now expected to return to school in one week.

Prophylaxis.—*Passive immunization* with about 3,000 units of enzyme-treated antitoxin injected intra-muscularly will confer a high degree of protection on Dick-positive subjects for two or three weeks at most. This method has a limited sphere of usefulness. Although sensitivity to serum has become much reduced by the use of enzyme-treated antitoxin it has not altogether ceased to exist. For this reason it is generally considered that serum should be reserved as far as possible for therapeutic purposes. *Active immunization* with Dick toxin is of value for Dick-positive reactors specially exposed to the infection, *e.g.* staffs of fever hospitals, or in a school or other semi-closed community when an epidemic threatens. It is rather a troublesome procedure and is not recommended for the general public in the present mild phase of scarlet fever. The dosage employed depends upon the size of the Dick reaction, very low starting dosage and slow gradation being used in those who are strongly positive. An average scheme of dosage is five injections at weekly intervals, *e.g.* 500, 2,000, 5,000, 20,000 and 50,000 skin test doses. After any of the injections the severity of the local reaction is the determining factor for the size of the next dose. If tolerance for the toxin is over-stepped at any stage, a scarlatiniform eruption ("miniature scarlet fever") will result. This has actually happened on an average in about 10 per cent. of those who have been actively immunized. If five injections are insufficient to make the Dick test negative one or two further injections of toxin should be given. The toxin has been given orally in keratin coated capsules, but this method is unreliable and very large doses are necessary (Dick and Dick, 1932). Toxoid has also been tried and found ineffective in about 50 per cent. of cases (Anderson, 1938). It should be noted that immunization against scarlet fever protects against the rash, but not necessarily (though probably partially) against upper respiratory hæmolytic streptococcal infections.

Quarantine period for Dick-positive contacts is one week. No quarantine is now imposed as a rule on adult contacts.

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DIPHTHERIA

Synonym.—Membranous croup.

Diphtheria is the reaction of the body to a virulent strain of *corynebacterium diphtheriæ*. It is characterized by local formation of membrane associated with relatively painless congestion and œdema, by generalized toxæmia and by liability to myocarditis and paralysis. Although it is one of the oldest epidemic diseases it was only in 1821 that it was distinguished as a separate disease by Bretonneau of Tours, who was also the first to perform tracheotomy in laryngeal diphtheria. Trousseau of Paris in 1825 demonstrated cutaneous diphtheria, the

paralysis and the general toxæmia. Intubation was recommended by Bouchut in 1857. Diphtheria was first differentiated from scarlet fever in the Registrar-General's returns in 1861. The bacillus was first detected by Klebs in 1875 in sections of the membrane, and in 1884 Loeffler cultured it and reproduced the disease in animals from his cultures. The exotoxin was discovered in 1889 by Pasteur's pupils Roux and Yersin, who obtained it by filtration of the cultures through porcelain. Diphtheria antitoxin was produced by Behring in 1890 ; its practical value in the human disease was demonstrated by Roux in 1894 and it was first used in England at the end of that year. Specific prophylaxis began with the intradermal test for immunity introduced by B. Schick of Vienna (1908–13), and Behring's use of toxin-antitoxin for immunization of human beings in 1912. Its employment on a large scale was due to Park and his associates (1923) of New York. Notable improvements in the technique of prophylaxis came with the production of " anatoxine " (formol toxoid) by Ramon in 1923 and of alum-precipitated toxoid by Glenny and his co-workers in 1926.

Epidemiology

The two chief factors which produce clinical cases of diphtheria are (1) the prevalence of virulent, and especially invasive, strains (*e.g. gravis type*), of the organism and (2) low levels of antitoxic immunity in the individuals exposed to them. The factors of age, sex, season and climate are subsidiary.

Age.—Under six months the disease is very rare. Under twelve months there are relatively few cases. The most common age group affected is two to six years, and the next most common six to ten years, after which there is a rapidly diminishing incidence with age. No age is altogether exempt.

Sex.—The disease is equally common in male and female children.

Season.—It is most prevalent in the autumn and winter months.

Distribution is world wide, but like scarlet fever, its incidence is greatest in temperate climates, and greater in cold countries than in the tropics. In England and Wales, in the decade before the opening of the immunization campaign in 1940, there were about 60,000 notified cases annually of which 3,000 died. In the years 1941 to 1951, the number of deaths fell progressively from 2,641 to 32. This is a high tribute to the immunization campaign when it is considered that during this period diphtheria deaths increased greatly in the non-immunized countries of Europe.

Transmission.—Droplet infection from cases or carriers is the chief mode of dissemination. Fomites, such as toys, utensils, towels, clothing, bedding and books can harbour the infection for long periods, since the organism resists drying, but their relative importance in transmission has not been accurately assessed. The bacillus can seldom be isolated from books handled by diphtheria patients (Lanbach, 1916). Milk contaminated by a case or carrier has in rare instances caused an epidemic. There is no bacteriological evidence that defective drains or sewer gas

ever give rise to diphtheria. In schools, children's institutions and wards infection may be spread by carriers or mild unrecognized cases, especially cases of anterior nasal diphtheria. Domestic animals, *e.g.* cats and birds, do not suffer from true diphtheria, and their rôle in transmission, if any, is similar to that of fomites (Rolleston and Ronaldson, 1940).

Incidence of toxic and of laryngeal forms.—The severe toxic or malignant form of diphtheria has considerably increased in certain parts of Europe, including Britain, since 1927. In the Virchow Krankenhaus, Berlin, the diphtheria death-rate rose from 5 per cent. in 1924 to 26·7 per cent. in the first five months of 1927 (Deicher). Similarly, in Leeds in 1931, the hospital case fatality rate for diphtheria suddenly rose from 4 to 14 per cent. due to an influx of malignant cases (Anderson *et al.*, 1931). So rapidly fatal were some of these cases that the value of antitoxin, even when given on the first day of disease, was questioned by certain observers (Leete *et al.*, 1933). Coincident with this rise in toxic diphtheria has been the marked decline in laryngeal diphtheria in the same areas and also a shift in the main age incidence from the one to five years group to the five to fifteen years group (Wright, 1941, Spörl, 1936). These changes are too great to be explained by the fall in the birth rate. They are more probably due to an increase in the toxic forms of bacilli, especially the *gravis* type. In U.S.A. such changes do not seem to have taken place or are inconspicuous, and malignant diphtheria is still relatively uncommon and laryngeal diphtheria frequent. Thus diphtheria in one place may be quite different from that in another, and in any one place may change naturally over a period of years (McLeod, 1943).

Bacteriology.—*C. diphtheriæ* grows most commonly on mucous membrane, forming a fibrinous pseudo-membrane which usually appears first on the tonsils. It may attack skin, for example, about the nares and lips in anterior nasal diphtheria, or as a secondary infection in wounds and sores, especially desert sores in the East. There is little evidence that it penetrates deeply into the tissues, although the gravis type ulcerates mucous membrane more deeply than mitis. It has very rarely been cultivated from the blood stream during life or from the organs of the body *post mortem*, except in the regional glands and spleen in hypertoxic cases. A degree of *local bacterial immunity* appears to exist in the respiratory mucous membranes independent of antitoxic immunity since susceptible animals with complete absence of circulating antitoxin can resist direct implantation of virulent bacilli on the untraumatized mucous membrane. Similarly Schick positive subjects may be carriers of virulent diphtheria bacilli without contracting the disease.

Biological types of C. Diphtheriæ.—In 1931, the Leeds workers distinguished the *gravis* and *mitis* types, and Mair (1936) drew attention to the *intermedius* or " barred " type. The main criteria for differentiation of these types are the colony form on tellurite media and the fermentation of starch. For example, on the original media used, the *gravis* colony is large, greyish, matt, with crenated outline like a " daisy-head," while the *mitis* colony is smaller, black, shiny, with smooth circular outline. *Gravis* ferments starch, *mitis* does not. *Intermedius* has intermediate colonial characters and, like *gravis*, is a starch fermenter. On the newer media, the colonies are different

but still quite distinctive, *intermedius* being much smaller than the others. The three types are serologically distinct and each contains a number of antigenic sub-groups. In England, the *gravis* type predominated in Yorkshire from 1930 to 1934 and later in Lancashire; *intermedius* still predominates in the South and West; there is a nest of *mitis* in Staffordshire. London has had a fairly even mixture of types in the last twenty years with *gravis* predominating. In Scotland, the *intermedius* type was known to predominate from 1934 to 1939 when a swing over to *gravis* took place accompanied by severer clinical forms of diphtheria. In Eire, *gravis* is markedly predominant in Dublin and Cork. In Africa, *mitis* is common, in Cape Town especially. In Canada, all three types have been recognized. In U.S.A. typical *gravis* strains are rare. In Australia, *gravis* is slightly predominant all over, with *intermedius* leading in Melbourne and absent in Adelaide. In central Europe *gravis* markedly predominates, especially in E. and N.E. and in Poland (McLeod, 1943).

The correlation of these types with clinical severity has been specially studied by McLeod. *Mitis* tends to grow only on the surface of the mucous membrane producing a firm opaque type of membrane without much œdema. It has a tendency to spread to the air passages producing laryngeal obstruction and pneumonia. Deaths from the *mitis* strain are mostly from this cause and occur chiefly in infants, because of the small diameter of their glottis and bronchi. *Intermedius* closely resembles *gravis* in producing severely toxic cases but the associated case fatality rate is less on the whole. Both *gravis* and *intermedius* tend to form thin filmy membrane in subjects with low immunity, to penetrate deeply into their tissues locally and into the cervical glands and periglandular tissue (clinically the "bull-neck" type). This is associated with great toxæmia, tendency to hæmorrhages and later to myocardial weakness and paralysis. *Gravis* strains have the greatest epidemic potency. The great majority of them are pathogenic to animals and a virulence test of *gravis* strains is therefore rarely required. *Gravis* rarely causes laryngeal diphtheria and pneumonia unless faucial diphtheria is present as well, but *intermedius* does so occasionally. Carriers are more frequent with *mitis* than with the other two, but *gravis* carriers are more persistent. Diphtheria in the immunized is nearly always due to *intermedius* and *gravis*. In Cork where *gravis* predominates the ratio of diphtheria in the immunized to the non-immunized is 1 in 5, and in Stafford where *mitis* prevails, it is 1 in 100. An apparent anomaly with *gravis* strains is that they are generally poor toxin formers in artificial media, although recently it has been found that good growth and toxin formation depend largely on the iron content of the medium.

Bacteriologically, therefore, diphtheria can be viewed not as one but as three closely allied diseases due respectively to *mitis*, *intermedius* and *gravis* types. In each case, the clinical picture is profoundly modified by the degree of immunity of the subject. With *mitis* the disease is nearly always mild or moderate, and tends to take the laryngeal form. *Intermedius* and *gravis*, on the other hand, produce all forms—the carrier state, mild, moderate or severely toxic diphtheria—according to the degree of immunity possessed by the patient when attacked. Thus mild cases of *gravis* infection (in spite of the name) are quite common in those with a fairly good level of immunity.

Although the above view is now widely held and is in accordance with clinical experience in Britain, some bacteriologists see the three main types merely as "smooth to rough" varieties of colony form such as characterize many other organisms. This school is not convinced that

toxigenicity and virulence are associated with any particular colony form or serological type (Morton, 1940).

Diphtheria toxin.—This potent diffusible tissue poison is responsible for practically all the symptoms of diphtheria except the mechanical ones, *e.g.* occlusion of the larynx, produced by the membrane and swelling. When injected intradermally (Schick test) it becomes fixed to the tissue-cells locally within three to six hours to such an extent that a moderate dose of antitoxin given intramuscularly after that time does not neutralize it, although a large intravenous dose may do so (Glenny and Hopkins, 1925). (This fact is utilized in the diagnosis of doubtful diphtheria, p. 1712.) The paralysis of the palate which may follow the acute stage of faucial diphtheria is probably due to direct diffusion of the toxin on to the motor nerve endings, since it always affects the side of the palate on which the membrane was most extensive. Most of the toxin produced at the site of the membrane is, however, rapidly absorbed into the blood stream and almost as rapidly taken up by the tissues of the body. The concentration in the blood stream, even in toxic cases, is never high. The amount of the toxin absorbed varies with the site, character and extent of the local lesions, being high from membrane in pharynx, palate, uvula and fauces, and low from membrane in larynx, trachea and bronchi. In the latter situations there is columnar epithelium, the superficial layers of which readily become detached from the basement membrane, and so lose contact with the circulation. Hence myocarditis and paralysis are common after faucial and pharyngeal diphtheria and rare after the laryngeal and tracheal form. The tissues most profoundly affected by the toxin are the heart muscle, adrenal cortex, renal tubular epithelium and peripheral nerves. The damage done by the toxin results in death or recovery which is apparently complete, at least in the young (p. 1709).

Symptomatology

The incubation period varies from two to six days. In most cases it is difficult to determine the exact moment of infection. The fauces, larynx and nasal passages are most frequently the primary seat of the disease. The membrane may be limited to one region or may extend from it or involve other organs simultaneously.

Faucial diphtheria

This may have an insidious or sudden onset. Young children often do not complain of sore throat. The faucial lesion may thus only be discovered by chance during a general examination. The importance of routine throat inspection in every medical examination for an obscure complaint cannot be too strongly emphasized. The first symptoms are usually malaise, peevishness, loss of appetite, headache and pains in the limbs. Vomiting is much less frequent than in scarlet fever. Constitutional disturbance is often slight in mild cases and the disease may be unrecognized for some days. The first throat sign is swelling and redness of the tonsils with membrane showing as small greyish white or yellow patches which are usually larger than the follicular deposits of a

streptococcal infection. They soon fuse into a plaque of membrane more or less covering the exposed surface of the tonsil. The redness of the mucous membrane in pure diphtheritic infection is duller and more localized around the area of the exudate than in streptococcal infection and the pain is not severe. At this stage an enlarged and *relatively painless submaxillary gland* on the affected side or sides can be easily palpated, and experienced observers also detect the odour of diphtheria. Further developments depend on the severity of the case. In mild cases (*faucial-tonsillar diphtheria*) the membrane within a few days loses its sheen, becomes opaque and " dead " ; its well-defined edge shrivels, curls up and separates ; then it breaks up and is shed. By this time the submaxillary adenitis has subsided. In moderate and severe toxic cases (*faucial-pharyngeal diphtheria*) the membrane extends *at least* over the faucial pillars, and any such extension forwards is usually associated with extension backwards to the pharynx. In the moderate cases the sides of the uvula and part of the pharyngeal wall are usually involved and there is an increase of *œdema* not only of tonsils but of fauces part of soft palate and uvula. The extending edge of the membrane may be pearly grey and shiny—an indication of a toxic case. The œdema in the throat has its counterpart in the neck, where the slightest amount of periglandular œdema (*periadenitis*) should be regarded as evidence of the toxic nature of the case. Fœtor in such cases is quite marked. A thin serous or blood-stained nasal discharge if present is typical of diphtheria. Membrane may be visible on the anterior part of the nasal septum or on the posterior pharyngeal wall behind the uvula.

Hypertoxic or malignant diphtheria.—In severely toxic faucial cases, all these signs are increased. The membrane extends on to the soft palate on one or both sides and usually covers part of the hard palate, uvula, pharynx and sometimes the nasal septum ; the tongue, the inside of the cheeks, gums, lips and floor of the mouth generally escape. The pharyngeal membrane can sometimes be seen protruding below the uvula but is usually hidden and its presence is evidenced by the thin serous or blood-stained discharge from the nose. The appearance of the membrane is characteristic of rapid spread. It is shiny and gelatinous, usually thin and may even be filmy and semi-transparent. This gelatinous or filmy character is best seen towards the spreading edge, where also there may be no clear line of demarcation between the membrane and the gross, painless, shiny œdema of the palate around it. In the neck, the œdema around the enlarged submaxillary glands forms the great, smooth, painless swelling known as periadenitis or " bull neck." The œdema is usually solid. It is of smooth circular outline, and the individual glands cannot be palpated through it. These signs are almost pathognomonic of toxic diphtheria. By the time they have appeared the typical fœtor of diphtheria is very strong ; the general signs of a depressant toxæmia are also marked ; the restlessness of the first day has given place to lethargy or drowsiness ; pyrexia is low or absent ; there is a waxy pallor, rapid feeble pulse and low blood pressure. The malignant cases have thus a characteristic clinical picture on the second or third day of disease which

it is essential to recognize without delay, since the life of the patient depends largely on immediate intensive intravenous antitoxin treatment (p. 1715). The child is pale and prostrate, lethargic or drowsy with rapid compressible pulse and pyrexia usually low; the mouth is open and breathing noisy; there is a strong odour typical of diphtheria; the membrane, nasal discharge, adenitis and periadenitis are as noted above.

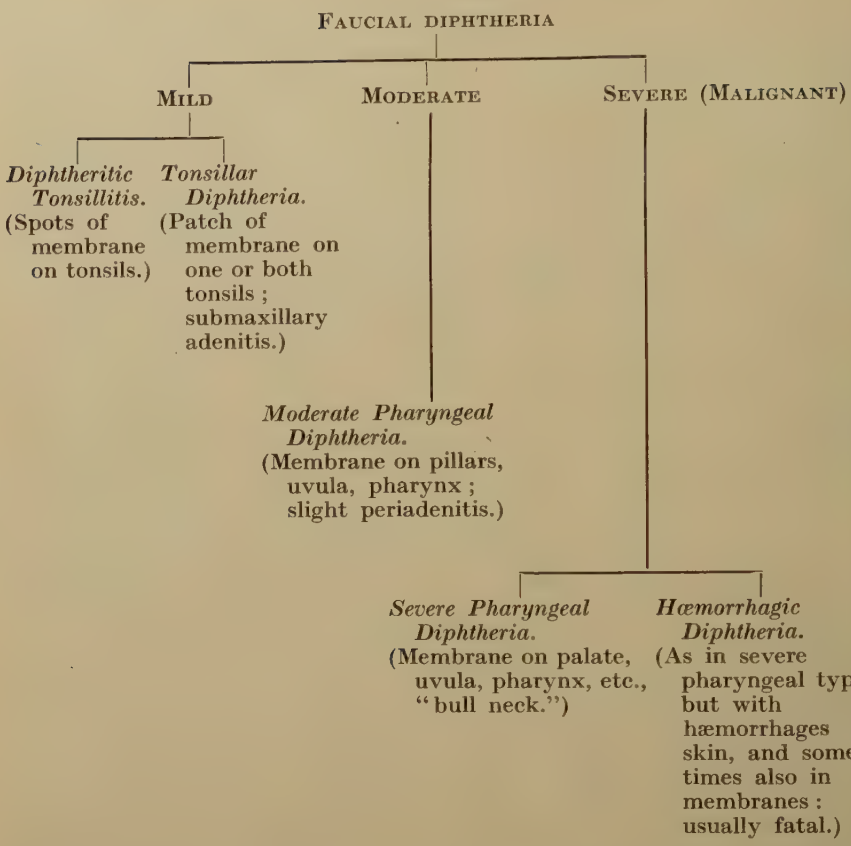
If the disease is allowed to run its natural course, decomposition of the membrane begins on the fifth or sixth day. After turning grey or black, according to the amount of hæmorrhage in it, it shrivels up and separates *en masse* or gradually disintegrates and comes away or is swallowed piecemeal. This process in untreated moderate or severe cases is usually accompanied by considerable hæmorrhage from nose and throat with occasional vomiting of altered blood. In the worst cases, petechiæ and purpuric patches appear in the skin and sometimes also in the mucous membranes (*hæmorrhagic diphtheria*). Almost all severe toxic cases, if untreated, are fatal within the first week or two, generally developing peripheral circulatory collapse and myocardial failure. With efficient antitoxin treatment, the process of separation of the membrane is hastened, hæmorrhage usually avoided and peripheral circulatory failure, myocardial weakness, and renal, nervous and muscular complications modified or even prevented. Even in the most favourable cases, however, it takes a few days for the membrane to separate and the underlying ulceration to heal.

Disappearance of the membrane merely marks the end of the acute stage. The illness is by no means at an end. The patient may still succumb from toxic complications and, in any event, must have some weeks or, in severe cases, even months of rest in bed; during the first six or seven weeks of this time the toxic effects are liable to appear.

Types of faucial diphtheria. It will be gathered from the above that faucial diphtheria may be classified for convenience into various clinical types according to severity. These types, however, overlap. The scheme on page 1706 represents such a classification in outline.

Laryngeal diphtheria is most often an extension from the fauces or pharyngeal wall (secondary form) but may arise independently (primary form). It is most common where *mitis* strains are prevalent and relatively rare when *gravis* strains predominate. It is much more common in children under six years of age than in older children and adults. In the latter it is nearly always of the secondary form, and usually the result of an error or delay in diagnosis, until the fifth day of disease or later, whereby faucial membrane is allowed to spread to pharynx, nose, larynx and bronchi. In older children, owing to the size of the larynx, signs of laryngeal obstruction are unusual. The most urgent symptoms of laryngeal diphtheria occur in infants and very small children.

In these the first sign is a barking or croupy cough and a muffled or lost voice and cry. Very quickly the breathing becomes stridulous; at first this may occur in spasmodic attacks, but within a few hours inspiratory stridor becomes continuous and ever more alarming. It soon becomes associated with recession of the lower intercostal spaces


FAUCIAL DIPHTHERIA
MILD
MODERATE
SEVERE (MALIGNANT)
Diphtheritic Tonsillitis. (Spots of membrane on tonsils.)
Tonsillar Diphtheria. (Patch of membrane on one or both tonsils; submaxillary adenitis.)
Moderate Pharyngeal Diphtheria. (Membrane on pillars, uvula, pharynx; slight periadenitis.)
Severe Pharyngeal Diphtheria. (Membrane on palate, uvula, pharynx, etc., "bull neck.")
Hæmorrhagic Diphtheria. (As in severe pharyngeal type, but with hæmorrhages in skin, and sometimes also in membranes: usually fatal.)

due to the diminished air entry, and, if unrelieved, the recession spreads to the lower ribs, the supraclavicular and suprasternal fossæ, and the sternum itself. By this time the child is cyanosed and very restless, sitting up in the cot at times to get more breath. This is the stage at which relief by operation becomes imperative. If relief is not obtained the heart soon begins to fail, pallor replaces cyanosis, restlessness gives way to exhaustion and death from asphyxia ends the scene. The whole process from onset to death may be over in less than twenty-four hours.

From the larynx, membrane spreads rapidly to *trachea* and *bronchi*, sometimes even to the smallest bronchioles in which case there is great liability to broncho-pneumonia. Membranous casts of the trachea and bronchi are not infrequently removed at the operation of tracheotomy or by larnygeal and tracheal suction.

Diagnosis in the primary form of laryngeal diphtheria is usually dependent on recognition of the above signs of laryngeal obstruction, since the fauces show little sign of inflammation and throat swabs may be negative. Proof of the diagnosis can only be obtained by inspection and swabbing of the larynx through the direct laryngoscope (p. 1718), a procedure which is usually reserved for the expert in hospital. Since it

is impossible by ordinary examination to distinguish between diphtheritic and other forms of inflammation causing laryngeal obstruction, all suspected cases should be notified and treated without delay as laryngeal diphtheria until the diagnosis can be confirmed or refuted.

The danger in primary laryngeal diphtheria arises almost solely from asphyxia and pneumonia. There seems to be relatively little absorption of toxin. Toxic complications are rare, even where there is extensive membrane lining the trachea and bronchi (p. 1712).

Nasal diphtheria.—This term leads to much confusion between two entirely different conditions : (1) *anterior nasal diphtheria* or *diphtheritic rhinitis*, a mild relatively non-toxic form in which the membrane is limited to the anterior part of the nasal septum, and (2) *posterior nasal diphtheria* or *pharyngeal diphtheria*, the most toxic form of the disease, in which the posterior part of the nose is involved along with adjacent parts of the pharynx, fauces and generally palate and uvula as well (p. 1713). Such confusion of terms may have serious consequences, since the prognosis and treatment of these two forms is as the poles apart. It is therefore desirable to avoid the term " nasal diphtheria."

Anterior nasal diphtheria occurs almost solely in children. Constitutional disturbance, pyrexia, shivering, etc., is slight or absent, and the child may be found attending school as usual. Locally there is (1) a watery or blood-stained discharge (purulent discharge may supervene later owing to secondary infection), (2) thick white membrane on the mucous lining of the anterior part of the nasal septum with a downward curved edge at its junction with the skin (this must be looked for with a good light ; it often passes unnoticed), and (3) redness, excoriation or crusted spots on the skin of the nares and upper lip (this is a form of cutaneous diphtheria due to infection from the nasal discharge and may not be present for some days after onset). The condition may be unrecognized for days or even weeks and may even clear up in some cases without treatment. In spite of its chronicity, paralysis or other toxic complication is rare.

Other mucous membranes less frequently involved are those of the eye, the middle ear, genitals and alimentary tract. In the eye a thin membrane can be seen lining the palpebral or ocular conjunctiva. If untreated with antitoxin the membrane may spread on to the cornea producing ulceration and ultimately corneal opacity and loss of vision. Diphtheria of the genital organs is more common in females, especially in young girls. The inner surface of the labia majora, labia minora and lower end of the vagina becomes covered with a grey membrane, the tissues become swollen, red and painful and there is fœtid discharge. The infection, like that of streptococcal vulvo-vaginitis, is generally transferred from a nasal or faucial lesion by means of the child's fingers. Toxic complications are unusual but paralysis of the bladder and rectum followed later by palatal and ocular paresis and weakness of the limbs has been reported (Leendertz, 1920). Diphtheria of the male genitals is very rare, and is limited to the prepuce. Most cases occur after circumcision and should, therefore, be more correctly classed as cases of wound

diphtheria. The œsophagus has occasionally been found involved at post-mortem examination when the faucial membrane is extensive. Other rare situations are the stomach, intestines and anus.

Cutaneous diphtheria.—The most common form is that noted under " anterior nasal diphtheria." The disease is also seen on the fingers, the back of the right hand, and the radial aspect of the right wrist and lower forearm. These are the areas usually contaminated in wiping the nose with the hand or arm. The lesions usually commence as small blisters or pustules which rupture leaving shallow crusted sores which do not respond to simple treatment. A rarer and very chronic form of cutaneous diphtheria results from secondary diphtheritic infection of wounds or sores, causing chronic ulcers with a dark scabbed and leather-like base. Diagnosis may only be made by lifting up the slough membrane and swabbing beneath it. Cutaneous diphtheria of this kind is not infrequently followed by paralysis. Diphtheria of the umbilicus can occur in new-born infants and others, but the great majority of cases are merely carriers of *C. diphtheriæ* which lives " extra-corporeally " in the secretions of the navel. Diphtheria of the middle ear (so-called) is usually a similar condition in which virulent or non-virulent diphtheria bacilli are existing saprophytically in the purulent discharge from the ear. It is exceedingly rare to find membrane in the middle ear or meatus.

Diphtheria in the immunized does not differ in any way from diphtheria in individuals who have attained a corresponding degree of natural immunity without active immunization. It is nearly always due to *gravis* or *intermedius* strains and, on the whole, is much milder than the disease in non-immunized children. The tonsillar membrane is frequently no more than a few specks of exudate.

In all forms of diphtheria, treatment by antitoxin leads to the separation or resolution of the membrane within a few days. This process is accompanied by a varying degree of ulceration of the underlying mucous membrane. In cases untreated by antitoxin, and, occasionally, in severe cases that are undertreated, membrane may be shed and re-formed repeatedly. In pre-antitoxin days this process was common until death or recovery terminated the illness.

Carriers.—A " carrier " is a person who harbours *virulent* diphtheria bacilli without exhibiting signs of the disease.

A *convalescent carrier* is one who harbours the organism as a sequel to an attack of the disease.

A *contact carrier* is one who has been in contact with infection from a case or another carrier. Contact carriers are common around a case of diphtheria but the condition is usually transient. Persons with healthy mucous membranes usually lose their infectivity within a week or two but may be re-infected transitorily from time to time. The chronic carrier frequently but by no means invariably has some abnormality of the naso-pharyngeal mucosa or its extensions, *e.g.* infected tonsils, adenoids or sinuses, trauma from a foreign body or some form of nasal obstruction. Appropriate treatment for this secondary infection is usually required before such carriers are cleared. A person from whom a single morpho-

logically positive swab has been obtained should not for that reason be called a carrier. Certain procedure is recommended on page 1721.

Clinical stages of the disease. The clinical course of the disease can be divided broadly into three stages. The *acute stage* occupying the first five to seven days has already been described. It is characterized by local membrane and general toxæmia. The second or *cardiovascular stage* lasts from about the fifth day to about the seventh week, with a critical stage in severe cases about the eighteenth day. During this stage myocarditis and peripheral circulatory failure are liable to appear and may be fatal. The third or *paralytic stage* lasts from about the third week to the end of the illness, which may be any time from the fourth week to the fourth or fifth month, according to the severity of the initial toxæmia. During this stage, circulatory improvement is usually taking place but various paralyses are liable to appear up to the seventh week. These stages are most obvious, and the third stage is longest in severe toxic diphtheria. In the milder forms, the second and third stages are often symptomless in well-treated patients. Even in toxic cases, all stages are profoundly modified by adequate antitoxin treatment.

Complications

Cardiovascular.—Circulatory weakness or failure is brought about by several factors. The initial general toxæmia, if severe, produces a condition allied to shock. There is an early tachycardia followed by pallor, low blood pressure and coldness of the extremities. This may be associated with general capillary leakage and diminished blood volume. In hæmorrhagic cases there is a leakage of red cells as well as plasma. Other possible factors involved are direct toxic action on the vasomotor centre and a deficient secretion of pressor substances by the adrenals. Histologically, however, the adrenal lesion in man is very slight. In the second stage systolic blood pressure may fall as low as 70 mm. Hg. This is usually accompanied or rapidly followed by signs of myocarditis. The myocardium may be affected both in its fibres and in its conducting system. The resulting cardiac weakness and irregularity may be accompanied by any of the following signs : weakness or muffling of the first sound at the apex, tic-tac sounds, re-duplication or splitting of first or second sound, displacement of apex beat downwards and to the left, gallop or triple rhythm and extra-systoles. The clinical and electrocardiographic signs usually correspond but in some grave cases the electrocardiogram may show little abnormal except *low voltage tracings*. In other severe cases the E.C.G. shows loss or impairment of conduction of all grades and types. These include complete heart-block, bundle-branch block, intraventricular block, auricular fibrillation and flutter, extrasystoles, and paroxysmal ventricular tachycardia. One of the most serious signs associated with cardiovascular failure is repeated vomiting—the so-called "cardiac vomiting of diphtheria." Extreme circulatory failure is always associated with oliguria and occasionally with anuria—a fatal sign. Cardiac vomiting is always serious and *the earlier it appears the worse the prognosis.*

There is a critical period about the eighteenth day. If cardiac weakness and vomiting first appear just a few days before that time, there is some hope, and if the patient survives the eighteenth day, recovery is usual.

Thrombi are occasionally formed in the ventricles of the heart when the circulation is very poor. These are the cause of *diphtheritic hemiplegia* or *pulmonary infarct* in certain patients surviving the critical period of the cardiovascular stage.

Peripheral nervous system.—The toxin has a special tendency to cause degeneration in certain peripheral nerves and their myelin sheaths, thus giving rise to diphtheritic paresis and sometimes to tingling and numbness. The exact route or routes by which the toxin reaches the nerves is not certain. Local or regional diffusion direct on to the motor nerve endings would seem to account for unilateral palatal paresis, which is always on the side occupied by the main mass of membrane in the acute stage. Blood dissemination of the toxin would seem a feasible explanation of the *polyneuritis* which is of later occurrence and is typically symmetrical. The toxin appears also to have a special affinity for the nerves of the palate, ciliary and external rectus muscles. These are the most common muscles involved after faucial diphtheria, and they may also be affected after extra-faucial diphtheria and accidental injections of toxin.

The magnitude and severity of the paralysis (and of all the toxic complications) depend upon the following factors : (*a*) the severity of the primary lesion, (*b*) the time elapsing between onset of the disease and antitoxin treatment, (*c*) the adequacy of the antitoxin treatment as regards dosage and route, and (*d*) the amount of rest or of exercise of the muscles during and subsequent to the acute stage. Paralysis is nearly always greatest in toxic cases, but may follow mild or ambulant cases in which diagnosis and treatment has been delayed. Severe toxic cases treated by large doses of intravenous antitoxin may be followed by surprisingly little paralysis. In the acute stage paralysis is rare and usually transitory (precocious paralysis). It has been known to occur in the palate, pharynx and facial muscles and may be due to direct attack of toxin upon those muscles.

Paralysis of the soft palate may be unilateral or bilateral and most commonly occurs in the third or fourth week but occasionally much later. The voice becomes nasal, swallowing of fluids may be difficult, and there may be regurgitation through the nose. The latter event is not commonly observed since the patient quickly learns how to avoid it. On inspection, the palate and base of the uvula is drawn to the affected side or the whole palate may hang immobile. Sensation and the palatine reflex may be impaired. In many cases the condition is a mild paresis and the only clinical sign a slightly nasal voice.

Ocular paresis.—*Ciliary paresis* quite frequently accompanies paresis of the palate and it may be missed unless accommodation is tested as a routine when the palate becomes affected. Paresis of *external ocular muscles* is less common ; usually the external rectus is involved, causing squint and diplopia.

The duration of palatal paresis is a few days to several weeks, and of ocular paresis about three weeks. Complete recovery takes place. Sensation of the buccal mucous membrane and even of the tongue, including the sense of taste, is impaired on rare occasions usually when extensive faucial membrane has invaded the buccal mucosa.

LATE PARESIS –PHARYNGEAL AND RESPIRATORY.—These are now rare events, even after severe toxic cases, provided that the latter are well treated with antitoxin. They usually appear late in the disease (fifth to seventh week) pharyngeal paresis being first. One or both lobes of the diaphragm are commonly affected, causing diminished air entry to the bases of the lungs, and some dyspnœa. Rarely the intercostal muscles also may show some degree of paresis. With pharyngeal paresis mucus collects in the pharynx. This mucus may be drawn into one of the main bronchi causing sudden collapse of a lobe and alarming dyspnœa. Inhalation pneumonia from food particles is another danger, since the intrinsic muscles of the larynx are also commonly involved in these cases. The respiratory difficulty throws a further strain on the heart which has usually by this time not quite recovered from toxic myocarditis. This combination of late pharyngeal and respiratory paralysis and cardiac failure is frequently fatal, especially in young children, unless the condition is very promptly treated by some mechanical respirator, *e.g.* the Drinker respirator, and by aspiration of the pharyngeal mucus by vacuum pump.

FACIAL PARESIS is uncommon ; it is of peripheral type although the part affected is usually that around the angle of the mouth.

PARESIS OF THE LIMBS due to peripheral neuritis is often not obvious as long as the patient lies in bed. There are various degrees of loss of power and sensation. Adults may complain of tingling and numbness, but children rarely do. In the worst cases, legs, arms, neck and trunk muscles may be affected. The knee-jerks are commonly lost, and often the ankle-jerks too. Various muscles, especially the tibialis anticus, are found to be weak. When the child gets up, he walks badly with a shuffling gait and with toes turned out. Acute flat foot may occur and require special treatment by massage and exercises to avoid permanent deformity.

Broncho-pneumonia is most likely to occur in laryngeal diphtheria with extensive tracheal and bronchial membrane or when there is pharyngeal and respiratory paralysis and food inhalation. **Secondary tonsillitis, cervical adenitis** or **acute otitis media** are evidences of secondary streptococcal infection, usually from other patients in a ward (p. 1688). **Albuminuria** is very common in the first and second stages of the disease in toxic cases, probably due to damage of the renal tubular epithelium. Occasionally in neglected diphtheria, untreated by antitoxin until a late stage, a toxic nephrosis may supervene, with œdema, heavy albuminuria and diminished ratio of albumin to globulin in the blood.

Herpes labialis occurs with diphtheria in about 4 per cent. of cases.

Purpura in convalescence is probably of similar ætiology to that of scarlet fever but rarer (p. 1690).

Relapses may occur after the third week of the disease ; they were formerly assessed at 1 per cent. In open wards a change of type of the infecting organisms in convalescent patients, *e.g.* from *mitis* to *gravis*, has frequently been noted, and as in scarlet fever (p. 1691) re-infection is probably the cause of relapses. In London, relapses were less than 1 per cent., possibly owing to the prevalence of *gravis* strains in the initial disease. Second attacks were estimated at about 2 per cent. They are due to slow and incomplete development of immunity in certain cases after an attack of diphtheria. The Schick test is not always reliable *after* diphtheria. In a small proportion of cases, a false positive reaction is obtained, due to sensitivity to the bacterial protein.

Morbid anatomy

In toxic cases, *post mortem*, most of the false membrane has usually separated, leaving an ulcerated hæmorrhagic bed. In laryngeal deaths there may be extensive membrane extending from larynx and trachea down to the smallest bronchi. Except over the vocal cords, it is usually loosely attached forming a sort of " inner tube." The *heart* is pale and flabby ; histologically the fibres may show no trace of damage or may, in early death, show focal areas of cloudy swelling, breaking up of nuclei, degeneration and even fragmentation of fibres. In these foci there is a secondary infiltration with lymphocytes and plasma cells and later histiocytes. After the third week the process of scarring begins in these foci with hypertrophied muscle fibres bearing enlarged and distorted nuclei, surrounding them. Focal lesions have been noted in the bundle of His and in the terminations of the vagus. The *kidneys* generally show a varying degree of cloudy swelling and toxic change in the epithelium of the tubules. The *liver* shows parenchymatous toxic changes. The *suprarenals*, in contrast with the gross hæmorrhagic lesions in the guinea-pig, frequently show little change beyond congestion and cloudy swelling. The *nervous system* constantly shows peripheral neuritis with myelin degeneration in the nerves supplying the paralysed areas. Histological research has failed to find central lesions (Uhry, 1933).

Diagnosis

The initial diagnosis (upon which a patient's life may depend) as distinct from a retrospective one, must be made on clinical grounds. In doubtful cases antitoxin should be given without waiting for a bacteriological report. Even when the first report is negative (*as not infrequently happens* e.g. *when the gravis organism is sown on Loeffler's and not on tellurite medium*) and the clinical condition still suggests diphtheria, antitoxin should be given. Many lives have been lost through the delay occasioned by swab taking. In doubtful and non-progressive cases, which can be kept under continuous observation, a Schick test should be done and antitoxin given after six hours if diphtheria still seems likely on clinical grounds. A moderate intramuscular dose of antitoxin will not then affect the result of the Schick test, and a solid retrospective diagnosis

can be made after a few days from clinical course, swab reports and Schick reaction.

The insidious onset of the disease makes it imperative to examine the throat of every ailing child, if diphtheria is not to be overlooked. Careful inspection in a good light is necessary, and the tongue must be depressed sufficiently to render visible the opposing faces of swollen tonsils and the posterior pharyngeal wall. Membrane on uvula, soft palate or faucial pillars strongly suggests diphtheria. These situations generally escape attack in other infections, except possibly in Vincent's angina and thrush which can be differentiated by other means. Limitation of exudate to one tonsil, the association of a unilateral blood-stained nasal discharge, signs of "croup" with a faucial lesion, are almost pathognomonic of diphtheria. *Painless periadenitis of the neck associated with relatively painless faucial œdema and exudate strongly suggests a severe toxic case.* False membrane varies greatly in appearance and extent according to the severity of the case (p. 1704).

Ulceration with muco-pus must be distinguished from membrane. The muco-pus and pultaceous exudate of other infections can be swabbed off without leaving a bleeding surface, while membrane tends to adhere and to bleed easily when swabbed. Whereas the absence of pain, moderate pyrexia and albuminuria are evidence in favour of diphtheria, other throat infections are usually associated with painful swallowing, high temperature, ulceration and sloughing of the fauces. A real difficulty arises when there is a mixed diphtheritic and streptococcal infection, a combination not infrequent. Here the various criteria of diagnosis must be individually assessed. It need hardly be said that signs of paralysis, the absence of a knee-jerk and evidence of cardiac dilatation are considerations that *never arise at the onset of the disease.* Their discovery can only lead to a retrospective diagnosis.

Differential diagnosis.—Faucial diphtheria has to be distinguished from various other forms of tonsillitis, scarlet fever, thrush and ulcerative stomatitis. In *acute follicular tonsillitis* the exudate is usually in the form of discrete soft greyish-yellow spots on the tonsils, but it may spread from the follicles in streaks or patches of soft pultaceous exudate covering the tonsillar surfaces. It does not, however, pass beyond the bounds of the tonsils, and it is generally easily swabbed off without hæmorrhage. The tonsils and the corresponding lymph glands are acutely tender and there is marked pain on swallowing. There is no periadenitis even in the presence of considerable faucial swelling. *Quinsy* is uncommon in children. It is usually unilateral; there is mesial protrusion of the tonsil and downward protrusion of the soft palate on the affected side; tenderness is extreme and trismus is common. *Vincent's angina* is a superficial ulceration of mucous membrane, commonly with greenish exudate and necrosis in the more severe cases. It is not very painful; there is little œdema, a foul odour, and usually some associated gingivitis or pyorrhœa alveolaris. Vincent's fusiform bacillus and spirillum are present in smears in *large numbers.* Small numbers in a clinically non-characteristic lesion have no special significance. *Agranu-*

locytic angina is a necrotic lesion associated with granulocytopenia and is usually subacute. *Pneumococcal pharyngitis* is a rare disease generally occurring in small epidemics due to a virulent strain of pneumococcus. There is at first grey shiny, glistening and later dark, dry necrotic exudate on uvula and soft palate more than on the tonsils. There is no marked fœtor. All swabs for *C. diphtheriæ* are negative. Pyrexia is high and constitutional disturbance severe (Henderson, 1934). *Ludwig's angina* is a cellulitis of fauces extending to the floor of the mouth and neighbouring structures. There is no distinctive exudate.

Scarlet fever is frequently mistaken for diphtheria (scarlet fever, p. 1693). The angina of *glandular fever* usually commences after a few days' malaise and posterior cervical glandular enlargement.

Thrush occurs in white well-defined patches on the buccal mucosa, fauces and tongue ; there is no accompanying redness or swelling ; smears of the exudate reveal *candida albicans*. *Ulcerative stomatitis* takes various forms, traumatic and infective. Infective lesions are usually small, discrete and scattered over the buccal mucosa, tongue, lips and gums as well as the fauces. Some of these ulcers are associated with Vincent's organisms, some with fungi, and some scattered discrete rounded ulcers, in infants especially, with the virus of *herpes febrilis* (primary herpetic fever (Scott *et al.*, 1941)). Recurrent *herpes* and tuberculous ulceration of the fauces are associated, with lesions elsewhere. *Sporotrichosis* of fauces, nares or eyes has been known to produce membranous lesions resembling diphtheria but without surrounding reaction (Banks, 1944).

Laryngeal diphtheria has to be distinguished from catarrhal laryngitis of bacterial origin, from obstructive symptoms due to foreign bodies, and from *acute laryngo-tracheobronchitis of presumed viral origin*. The latter, if untreated, runs a relatively long acute course with bouts of dyspnœa from croup, usually without loss of voice, and is often fatal. Autopsy shows hæmorrhagic tracheal and bronchial exudate and hæmorrhagic pulmonary œdema.

Prognosis

This varies according to the age of the patient, the site, character and extent of the membrane, the length of time which has elapsed between onset and specific treatment, and the adequacy of the dosage and route of the antitoxin. The younger the patient, *ceteris paribus*, the more serious the prognosis. Toxic diphtheria at age three to seven years is more often fatal than a similar condition at age ten years or more. The fatality of diphtheria varies greatly from place to place and from time to time in the same place (p. 1701). The day of disease on which serum is given is a most important factor. If it is given on the first day fatality is very small, but it increases with each subsequent day. Large doses, *e.g.* 100,000 to 200,000 units intravenously, can save many lives in severe toxic diphtheria, that would be lost if smaller and intramuscular doses were given. But, once the toxin has been absorbed from the circulation and has produced degenerative changes in the cardiac muscle and nervous tissues, no amount of antitoxin can undo the mischief.

Thin, glistening, ill-defined membrane rapidly spreading over the faucial pillars, uvula, soft palate and pharynx with much œdema is much more serious than thick, dull, well-defined membrane limited to the tonsils and without much surrounding œdema. Periadenitis which will be present in the former case and not in the latter is also of serious import. Petechial hæmorrhages, unless they occur twelve hours or more after adequate antitoxin, practically always indicate a fatal degree of toxæmia. Heavy albuminuria is unfavourable; anuria is almost always fatal. Waxy greyish pallor suggests grave toxæmia. Slow resolution of the membrane and of the periadenitis of the neck are unfavourable factors. The earlier the onset of circulatory failure, *e.g.* from fifth to twelfth day, the worse the prognosis. Concomitant vomiting is a grave sign (p. 1709). Respiratory and pharyngeal paralysis, at fifth to seventh week, were formerly frequently fatal, but the Drinker respirator has saved many lives in such cases.

In laryngeal cases, the chief danger is from asphyxia and bronchopneumonia, not toxæmia. The ultimate prognosis of myocarditis and paralysis, at least in the young, is good. If death is avoided in the critical periods of the acute, the cardiovascular, the paralytic and the convalescent stages recovery of heart and neuromuscular system appears to be complete except in the rarest instances.

Treatment

The two cardinal principles which govern the treatment of diphtheria are the administration of adequate antitoxin at the earliest possible moment, and rest or modified activity, appropriate to the degree of toxicity of each case.

Antitoxin.—The dose of antitoxin required is not proportional to the age of the patient, but is dependent on the site and severity of the lesion, the degree of toxæmia and the day of the illness. *The aim should be to give all the antitoxin required in a single dose.* A second dose is only required when, after twelve to twenty-four hours, it is seen that the membrane is still actively spreading. In practice this is not infrequent —an indication of the difficulty of accurate assessment of the first dose. In mild tonsillar, anterior nasal, laryngeal and non-respiratory cases, conditions in which there is relatively little toxæmia, 8,000 to 20,000 units intramuscularly is sufficient. Where the membrane invades the faucial pillars or sides of the uvula or is seen on the pharyngeal wall and especially if there is any associated periadenitis, the case must be considered moderately toxic, and the appropriate dose is 20,000 to 100,000 units intravenously. If the membrane is spreading over the soft palate and is accompanied by much œdema and periadenitis (" bull-neck ") the case is severely toxic and the appropriate dose is 100,000 to 200,000 units intravenously. The aim is to reverse toxic damage as far as possible, as well as to neutralize toxin which may still be absorbed from the site. The former requires an immediate and relatively enormous concentration of antitoxin in the blood.

Intramuscular injection is best given in the vastus externus muscle. Intravenous injection in severe cases in young children is technically difficult. It is essential to have a sharp needle with a short bevel (2·5 mm.) and syringes with peripheral nozzles. In children under six years, the external jugular veins are more convenient to inject than the antecubital.

Serum reactions have been nearly abolished by the use of the best enzyme treated antitoxin. Apart from true anaphylaxis, which is very rare, two reactions are possible after intravenous injection: (*a*) an immediate anaphylactoid or shock reaction, and (*b*) chills or thermal reaction about three-quarters of an hour after the injection. With the new antitoxin both are now rare, particularly (*a*), which was formerly a dangerous reaction and quite common. Nevertheless special precautions are still necessary after intravenous injection of antitoxin (p. 1695).

Dextrose therapy.—Disorder of carbohydrate metabolism occurs in diphtheria as in most fevers. Toxic cases may show a low blood sugar tolerance curve. It is desirable to give dextrose freely in all drinks, and it is a good thing to give it intravenously also along with the antitoxin if possible. Formerly insulin was given along with dextrose for about ten days in the acute stage, but this has been given up since a controlled experiment showed that it had no apparent influence on the course of the disease (Begg, 1935). The administration of dextrose intravenously must be considered of secondary importance to the adequate administration of antitoxin. In severe cases in young children, one is faced with the practical problem of administering a certain amount of fluid (antitoxin) intravenously without delay and often under difficult conditions. The essential point is to secure the injection of an adequate amount of antitoxin by this route, preferably without damaging all accessible veins since further intravenous injections may be required. If, in spite of these difficulties, 20 to 50 c.cm. of 50 per cent. dextrose can also be given intravenously so much the better. When given at an early stage, this hypertonic solution may have some effect in reducing the great œdema of fauces and neck.

Rest.—This is the second cardinal principle in treatment. The mildest clinical case of diphtheria should be in bed for at least three weeks, and thereafter the return to normal exertion should be gradual over a period of some weeks. Severe toxic cases which recover will usually require to be in bed for twelve weeks or more, the time depending upon the degree of myocarditis and paresis which becomes manifest. Thereafter a period of six to twelve weeks is usually required during which exercise is gradually increased up to normal activity. Cases intermediate between these two extremes require periods of recumbency and rest appropriate to their severity. Care should be taken that a patient does not undergo sudden or sustained physical strain during the period of rest, *e.g.* sitting up suddenly, reaching out to a locker or getting up and walking too soon. A flat pillow in the early stage usually conduces to less physical strain than no pillow at all. Pillows are added gradually, beginning from the third to the eighth week according to severity after

which the patient is allowed up in blankets for a few days and finally in clothes. Reading is restricted but not prohibited in the first four to six weeks unless ocular palsy sets in.

LOCAL TREATMENT.—This plays a minor part. No special treatment of the fauces is necessary. Gentle swabbing of mouth, tongue, gums and lips and inunction of the latter with boric ointment is a routine in the acute stage of all severe fevers.

CHEMOTHERAPY.—Penicillin and sulphonamides have a place in the treatment of the acute stage whenever secondary infection with hæmolytic streptococcus and certain other organisms is prominent. These drugs are especially valuable after *tracheotomy*, in order to keep the tracheal and bronchial mucous membranes clear of secondary infection and so promote rapid resolution and healing.

In hypertoxic diphtheria there is no clear evidence that combined antitoxin and penicillin is more effective in saving life than antitoxin alone. There is no doubt, however, that penicillin keeps down secondary organisms, and prevents purulent secretion and sloughing. From this point of view it is a considerable gain. It must be given in doses, of at least $\frac{1}{2}$ million units daily for four or five days.

The most suitable preparation is procaine penicillin, since the intramuscular injections can then be given in a depot dose at twelve or twenty-four hour intervals. More frequent injections often do more harm than good in such a toxic state, since they disturb rest and sleep.

In moderate and mild forms of faucial diphtheria, penicillin is not specially indicated except in case of secondary infection.

In *convalescent carriers* penicillin in the same dosage will produce negative swabs at least temporarily in about two-thirds of the cases. It is probable, however, that only the superficial organisms are killed and that diphtheria bacilli persist in some cases deep in the crypts of the tonsils. For such cases, tonsillectomy may be indicated if the tonsils are ragged and diseased. The carrier problem should, however, always be viewed in relation to immunization. In a well immunized community carriers are harmless and even beneficial as a means of stimulating further immunity.

DIET AND GENERAL MEASURES.—Fluids or semi-solids are given in the early acute stage. As soon as solid food can be tolerated it should be given. Vitamin B_1 like other vitamins is desirable in the diet. There is no sound evidence, however, that it has either a prophylactic or curative effect in diphtheritic paralysis (Wassermann, 1946).

In threatened circulatory failure, warmth, dextrose drinks restricted to sips of fluid if there is vomiting, intramuscular injections of adrenal cortical extract six-hourly and oxygen by tent or mask are the chief measures. The value of cortisone is yet to be determined. In severe palatal and pharyngeal paralysis and after tracheotomy when dysphagia is present, nasal feeding is often necessary. If saliva and mucus collect in the pharynx, the foot of the bed should be raised and the mucus sucked out at intervals by a vacuum pump. About the fifth to seventh week sudden dyspnœa (collapse of a lobe) or more gradual failure of abdominal

respiration or recurrence of myocardial signs indicates that respiratory paralysis is present or imminent and the patient should be moved immediately into a Drinker's apparatus or some other form of mechanical respirator.

Physiotherapy.—For paresis of the limbs, neck or trunk, massage and radiant heat and general ultra-violet light baths are useful in the convalescent stage. They are specially indicated in severe multiple paresis and in acute flat foot consequent on paresis of the tibial muscles.

Special treatment in other forms of diphtheria.—In anterior nasal diphtheria simple nursing toilet of the nose and surrounding skin and in diphtheria of the eye and vulva antibiotics are indicated. Antitoxin should never be applied to membrane locally. In *laryngeal diphtheria*, warmth, hot fomentations or poultices to the neck and a steam tent often allay the accompanying spasm and may avert operation. If the child becomes restless and has spasms of dyspnœa and cyanosis, and if there is marked recession of the chest-wall, operative measures are required. The operation of choice is direct laryngoscopy and aspiration of membrane with a powerful suction pump repeated at intervals as necessary. By this means the membrane as it loosens can be removed piecemeal. Casts of the whole larynx and trachea are sometimes removed. This procedure frequently saves the patient from the hazards of emergency tracheotomy. If the obstruction is due to œdema rather than membrane or, if the patient is at the point of suffocation, tracheotomy is the operation of choice. After the incision is made in the trachea the insertion of the tube is facilitated by the use of a hollow pilot tube with obturator openings (Luer or Park Hospital type). Intubation although effective at the time has the great disadvantage that the tube is easily coughed out. If it is used, the most harmless method of inserting the tube is through the laryngoscope under direct vision.

The Schick test

This is an intradermal test of the immunity type (in contrast with the tuberculin test which is of sensitivity type). A standard amount of diphtheria toxin contained in 0·2 c.cm. (the amount now fixed was based on combining power with antitoxin as well as on toxicity; it is only approximately $\frac{1}{50}$ M.L.D.) is injected intradermally in the front of the *left* forearm and a similar dose, previously heated to destroy the toxin, is injected as a control in the right forearm. If the person tested is susceptible to diphtheria, a circumscribed area of redness 1 to 2 cm. in diameter, with slight infiltration of the skin, appears *after* twenty-four hours on the test arm (left), whilst the control arm (right) shows no change. This is termed a *positive reaction* and, typically, it reaches its maximum by the third or fourth day and then fades, leaving a brown pigmentation and desquamation which may last for several weeks. No reaction in either arm after three days indicates that the individual is immune to diphtheria (*negative reaction*). The Schick reaction has been found to vary roughly in inverse proportion to the amount of antitoxin in the peripheral circulation. A marked reaction indicates very low blood antitoxin; a negative reaction

is believed to indicate neutralization of the injected toxin by the antitoxin present in the blood. A Schick negative individual certainly has immunity of a high but not absolute degree. Such persons subjected to massive doses of an organism with highly invasive properties, *e.g. gravis*, sometimes contract diphtheria, which, however, is nearly always mild. The level of Schick immunity in man lies between $\frac{1}{500}$ and $\frac{1}{250}$ unit of antitoxin per c.cm. of serum (Parish and Wright, 1935). In individuals with less than $\frac{1}{500}$ unit the Schick test is nearly always positive; with more than $\frac{1}{250}$ unit it is nearly always negative; between those limits the reaction may not be clear cut. The correspondence between Schick tests and blood antitoxin content is only approximate. *False positive reactions* (of sensitivity type) are very rare in children in primary Schick testing, but may occur after an attack of diphtheria even in children.

The solution of toxin employed for the Schick test cannot be obtained pure. It contains some protein derivatives of the medium and of the bacteria themselves. These antigens produce a local sensitivity reaction in certain persons, chiefly those who have had much contact with the diphtheria bacillus and have a high degree of antitoxic immunity. This sensitivity or pseudo-reaction must be distinguished from the true Schick reaction. It appears earlier, usually in about eighteen hours, reaches its maximum in about twenty-four hours and disappears by the fourth or fifth day leaving no desquamation. Persons who are sensitive to this protein will show either the *pseudo and negative reaction* (a more or less equal pseudo-reaction on both arms) or the *pseudo and positive* (*combined*) reaction (a reaction on both arms, that on the test arm, however, being larger, lasting longer and leaving some desquamation). The pseudo and negative reaction is much more common than the pseudo and positive. Great care must be taken in reading a pseudo-reaction. All doubtful cases should be checked by a blood test for antitoxin content. It is a great mistake to attempt to immunize persons with a pseudo and negative reaction. They react badly to immunization and do not need it, as they are usually highly immune. Pseudo-reactions are rare under eight years of age.

Immunity depends, however, not only on the amount of natural antitoxin in the blood, as shown roughly by the Schick test, but on the capacity to produce antitoxin rapidly in response to infection. Thus in certain persons who have had the disease or who have undergone latent immunization by natural means or been artificially immunized, the antitoxin in the blood sometimes falls to a low level. These persons seldom, however, contract the disease since the least exposure to infection, or even the stimulus of a Schick test, rapidly raises their antitoxin level.

Age and immunity.—The result of the Schick test shows a fairly constant variation with age and degree of exposure to diphtheria infection. About 80 per cent. of infants under three months give a negative Schick reaction. The immunity at this age is passive, antitoxin having passed the placental barrier from mother to fœtus. That this passive immunity lasts longer than usual is probably due to the antitoxin being attached to homologous protein. Antitoxin in colostrum and milk is most

probably digested and destroyed. At the age of six to twelve months antitoxin is low or even absent from the blood, but thereafter tends to increase rapidly with age in response to small infections, the natural disease, or active immunization. At the age of one year about 90 per cent. are Schick positive in most countries; at two years about 80 per cent., although there is considerable variation. From that age onwards there is a steady increase of immunity, but less in children of the well-to-do than in the children of the poor. The former presumably have less chances of meeting infection: at the age of twenty years only about 50 per cent. of them are immune, whilst at that age amongst the poorer classes as many as 85 per cent. may be immune. These figures do not apply to populations highly immunized artificially. Thus the percentage of immunes at given ages varies as between rural and urban districts and as between one area or country and another.

Immunity after diphtheria.—The Schick reaction is positive during the acute stage of diphtheria, and generally for a considerable period thereafter. About 50 per cent. of convalescents at the time of their discharge from hospital are still Schick positive. Immunity, however, usually develops slowly during the succeeding few months. A certain number remain Schick positive for long periods, but they seldom contract a second attack. Some of these may be false positive reactions.

Prophylaxis

Passive immunity can be produced in twenty-four hours or less by the intramuscular injection of about 2,000 units of antitoxin; this immunity lasts only three to four weeks and may sensitize the individual to further doses of serum, although with enzyme-treated antitoxin this risk is small. *Passive active immunity* can be attempted by the simultaneous injection of 500 units antitoxin and 0·2 c.cm. A.P.T. followed by 0·5 c.cm. A.P.T. four weeks later. This method gives passive immunity for the first three weeks followed by active immunity which, however, is somewhat delayed and weakened as compared with that following the use of A.P.T. alone. Immunity would tend to be deficient about the period three to six weeks after the combined injection (Downie and others, 1941). Ramon's original method of commencing the A.P.T. injections two weeks after the serum injection is to be preferred.

Active immunization.—The aim of hygienists is the universal immunization of children against diphtheria, from the age of about nine months. A preliminary Schick test may be done in individual cases, but in mass immunization it is hardly worth the trouble in children under nine years of age. The antigens now in common use in this country are alum-precipitated toxoid (A.P.T.) or the improved product precipitated by alum phosphate (P.T.A.P.) and toxoid antitoxin floccules (T.A.F.). The method of choice for young children (up to three years) is by two doses of 0·5 c.cm. P.T.A.P. intramuscularly or subcutaneously at four weeks' interval, and for older children and adults 0·2 c.cm. followed by 0·5 c.cm. P.T.A.P. after four weeks. A high Schick reversal rate of 95 to 100 per

cent. in one to three months after completing the course can be obtained by this method. Pseudo reactors to the Schick test and certain other persons are apt to have severe local and even general reactions. For them, the doses should be reduced or, alternatively, T.A.F. in three doses or more of 1 c.cm. at three-weekly intervals may be used. Objections to T.A.F. are that it contains a small amount of toxoid and is therefore less potent as an immunizing agent than A.P.T. and that the minute amount of antitoxin in it seems to sensitize to serum much more than a therapeutic dose. Active immunization between two and six months of age is possible unless the infant possesses a high level of natural antitoxin. In a well immunized country immunization under six months is rarely necessary. A boosting dose of 0·5 c.cm. P.T.A.P. should be given after one to two years to all children immunized under three years of age.

Combined immunization.—Active immunization against two or more diseases by simultaneous injection of toxoid and a bacterial vaccine has been shown to lead to higher antibody formation than injections of the antigens singly (Ramon, 1939). A convenient combination for young children of nine to twelve months is a potent pertussis vaccine and A.P.T. in two doses at four weeks' interval, followed by at least one further dose of the vaccine. Reactions may be severe, however, and neither this combination nor intra-muscular injection should be used during an epidemic of poliomyelitis, since there seems to be some danger of post-inoculation poliomyelitis affecting mainly the arm injected (Martin, 1950).

Control of institutional epidemics

The best method of control of diphtheria in children's institutions is to have every child and every adult in attendance Schick tested, and, if positive, actively immunized. In such circumstances, persons found to be carriers should be ignored. When diphtheria breaks out in an institution the following procedure is recommended : (1) all clinical cases are to be removed at once to the fever hospital ; (2) a swab of nose and throat is taken from all contacts ; (3) all contacts are Schick tested ; (4) those with morphologically positive swab reports are isolated together until the virulence test has been done ; (5) those with non-virulent bacilli in the swabs are released from isolation ; (6) those with virulent bacilli in the first swabs have a second swab taken of nose and throat ; (7) if the second swabs are negative (as frequently happens with contact carriers) the individuals concerned are released from isolation ; (8) those who have a second swab positive should be transferred to a fever hospital as carriers ; (9) all Schick positives should be actively immunized. By this procedure the occurrence of new cases of diphtheria will soon be checked by the active immunization, and many unnecessary admissions of transient carriers to the fever hospitals will be avoided. Unless more than one case of diphtheria occurs, elaborate measures are seldom required in these days of widespread immunization.

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MEASLES

Synonyms.—Morbilli; Rubeola. *Fr.* Rougeole, *Ger.* Masern, *Ital.* Rosolia, *Span.* Sarampion, *Dutch.* Mazelen.

Definition.—Measles is characterized by a prodromal catarrhal stage during which Koplik's spots appear in the mouth, a generalized macular and blotchy rash, liability to broncho-pneumonia in young children and intense infectivity in the prodromal and early eruptive stages.

Epidemiology.—The disease occurs all over the world: no race is immune. It may completely disappear for long periods from isolated communities and re-appear among the non-immune population as a devastating epidemic. In this country and most populous places it is endemic. In large cities like London and New York, epidemics occur with great regularity every two years, although certain factors occasionally upset this rhythm, *e.g.* the evacuation of children from London in 1940. The periodicity of epidemics is probably due to the gradual re-accumulation of susceptibles, chiefly among children born since the

previous epidemic who have lost their inherited immunity (Greenwood and Topley, 1936), and among older children who have lost their latent immunity acquired in previous epidemics (Stocks and Karn, 1928). In smaller towns and more scattered communities the biennial rhythm is less regular than in the large cities.

Season.—The seasonal incidence is in winter and spring. Rarely it extends throughout the summer as in London in 1941 when evacuated children were returning in large numbers. The peak incidence in epidemics in this country occurs in late March and the peak mortality a week or two later; the latter follows closely the curve of mortality from broncho-pneumonia. Mortality is highest in the North and Midlands and lowest in the South (Brincker, 1938). Since 1920, there has been a rapid fall in the death-rate from measles in this country, and from 1942, a still more significant decrease probably mainly attributable to sulphonamides and penicillin.

Age.—Congenital measles is known in rare instances in which infants are infected from non-immune mothers who develop the disease about the time of confinement. In the first three months of life measles is exceedingly rare, at least in recognizable form, owing to passive immunity transmitted through the placenta. From three to five months measles is still very rare and clinically mild. Subclinical forms may occur at this age and may play a part in the immunization of individuals who reach adult life without contracting measles in spite of many exposures to infection. From five to eight months it occurs much more commonly but is still modified; after the age of eight months the passive immunity has waned and attacks are unmodified. The period of highest fatality is nine months to two years. After three years of age, fatality rapidly decreases and after five years is negligible. All this applies only where measles is endemic and is contracted by almost the whole population. Among populations in which measles has been absent for a generation or more, *e.g.* in remote islands, adolescents and adults may be attacked as frequently as children. This is a characteristic feature of a "new" epidemic disease.

Transmission is by droplet spray or air-borne "droplet nuclei" or dust from the time of the first symptom until the rash but not the staining has faded, that is, a period of approximately eight days. Infectivity is extremely high amongst susceptibles, especially those in a limited area around the source of infection. There is no evidence that the virus survives long outside of the body, either in the air or on the clothing, etc. In institutional outbreaks, where exposure is less intimate than in the home, it has been estimated that exposure fails to produce an attack in about 25 per cent. of susceptibles.

Immunity is generally permanent following the unmodified disease, and, as far as is known, following modified attacks also. Second attacks are probably much rarer than is commonly alleged owing to confusion in diagnosis, *e.g.* with rubella.

Bacteriology.—The causal organism is a virus which is present in the naso-pharyngeal secretions and the blood at least twenty-four hours

before the rash and for a day or two after its appearance. The disease has been transmitted to monkeys by inoculation with these fluids during this period. Stokes and others have grown the virus on the chorioallantois of the developing chick embryo and with it have reproduced the disease in susceptible children by inhalation and inoculation (Stokes, 1943). The virus antigen has been used by Maris and others (1943) for prophylactic inoculation, but so far, protection against measles has not been complete in the inoculated children. The antigen may be used for a serological test of antibody in man.

Symptomatology

The incubation period is usually ten or eleven days, but it may vary from seven to twenty-one days. Prolonged incubation periods are common in serum-attenuated measles (p. 1731).

The prodromal stage, from the onset of symptoms to the appearance of the specific eruption on or about the fourth day, is the most infectious phase. It is characterized by pyrexia, often with a remission on the second or third day, prodromal rashes in some cases, Koplik's spots in about 80 per cent. of cases and catarrh of mucous membranes of eyes, nose, sinuses, middle ear cleft, cheeks, lips, gums, pharynx (slight), larynx, trachea, upper bronchi and alimentary tract. The *prodromal rashes* which appear in the first two days in the form of a blotchy, urticarial, macular or punctate erythema, are usually fugitive and localized. *Koplik's spots* are pathognomonic of measles. They appear one to three days before the rash. They require a bright light for their detection since they are *minute*, more pin point than pin head in size, like grains of salt on a red base. They are bluish white in colour and surrounded by a red areola in the earliest stage. As, or soon after the true rash appears on the skin, the Koplik's spots fade, leaving a characteristic extremely fine granularity on the surface of a uniformly reddened mucous membrane. They are most frequently seen on the buccal mucosa opposite the lower molars and, if numerous, also inside the lower lip. They have been noted on the plica semilunaris and caruncle of the eye, on the tracheal mucous membrane at autopsy and on the colon at operation. They are composed of degenerated mucin-containing cells situated around the duct of a submucous gland. They can be partly obliterated by repeated pressure with the spatula during examination. They must be distinguished from thrush, aphthous stomatitis, small dental traumatic ulcers, relatively large yellowish spots of submucous fat, small air bubbles and particles of food or inspissated mucus. The *catarrh* of measles is usually accompanied by lachrymation photophobia, nasal discharge, a short cough and sneezing; occasionally an early, pre-eruptive, laryngitis appears with hoarseness, croupy cough or stridor, and this may progress to intercostal recession and dyspnœa requiring tracheotomy. In small children, catarrh of the intestinal tract may give rise to diarrhœa. This is usually transitory but occasionally persists as a serious complication. Adenitis and enlargement of the spleen are much less prominent than in rubella. The *blood picture* at this

stage shows a slight neutrophil leucocytosis and some degree of secondary anæmia. When the rash appears, the leucocytosis is replaced by leucopenia.

Eruptive stage.—The characteristic *rash* appears on the third or fourth day behind the ears, on the sides of the neck, around the mouth and on the forehead ; it quickly spreads over the face, neck and the front of the chest. This earliest stage of the rash usually consists of discrete pinkish macules or small papules, quite sparse on face and chest resembling the rash of rubella. Within twenty-four hours, the rash becomes much more profuse, spreading over face, trunk, upper and lower limbs in successive crops. Its character also changes. The papules are larger, coarser, dusky or brick red in colour, irregular in size and shape, fused in places into crescentic or amorphous blotches or even into large confluent patches in areas subjected to pressure, *e.g.* on the back and buttocks. The coarse rash on the face and the marked conjunctivitis give the patient a characteristic bloated and bleary appearance. The rash tends to aggregate also on any site of inflammation or irritation, *e.g.* eczema, intertrigo or lymphangitis. The eruption lasts usually four or five days, but its duration may be as short as a few hours in mild or attenuated (p. 1731) cases. There is always some degree of capillary leakage of blood in the coarser papules and as the rash fades, this causes the characteristic " post-measles staining " which is not obliterated by pressure and varies from a massive purplish coloration of the skin to a brown or faint grey mottling. It may enable a retrospective diagnosis of measles to be made. Coarse purplish rashes followed by intense staining are frequently seen in measles of ordinary severity and do not usually indicate severe toxæmia. The staining gradually disappears in a few days.

As the rash develops, the temperature rises, the catarrhal signs increase and the patient feels ill and miserable. Pulse and respiration become accelerated, rhonchi may be heard in the lungs, the urine is concentrated and there may be diarrhœa. A diagnosis of pneumonia is frequently made at this stage, although within two or three days, without special treatment, the temperature falls, the rash fades in the order in which it developed, and all symptoms rapidly abate. A short, moist or sometimes hoarse cough or mucopurulent nasal discharge may persist for a week. Desquamation is often absent or may be of a fine branny character from sixth to eighth day on face and neck, waist or body but not on the palms or soles. It is naturally greatest when minute vesicles have appeared in the elements of the rash (morbilli vesiculosi). Serial X-ray films of the chest in the pre-eruptive and eruptive stages showed in 25 to 40 per cent. of a series of 130 cases pneumonic infiltrations of light density. In many of these cases physical signs of bronchial or pulmonary involvement were absent. Autopsy on a child who died three hours after the appearance of the eruption showed distinct round-celled peri-bronchial infiltration (Kohn and Koiransky, 1929).

Varieties of measles.—Although measles varies less than other exanthemata in clinical severity, there are times when the prevailing type is mild, and times when it is severe and frequently complicated by pneumonia, as in London in a succession of epidemics prior to 1936.

Mild types.—Individual cases have been described with all the symptoms, including Koplik's spots but without the eruption. When the disease prevails in summer, as in London in 1941, cases tend to be mild. The mildest cases, however, are seen in the " attenuated measles " produced by prophylactic injections of convalescent or adult serum, placental extract or gamma globulin. In the mildest form of " attenuated measles," the incubation period is prolonged, sometimes up to twenty-four days, the prodromal stage shows little or no constitutional disturbance or fever, only a mild short cough and usually no Koplik's spots. The eruption is limited to a few pink papules generally confined to the trunk. These fade in about two days and this marks the end of the illness. Even such mild clinical phenomena appear to produce permanent active immunity. All gradations of attenuated measles, of course, occur from this minimum up to the barely modified disease, according to potency, dosage and time of administration of the immune serum or its equivalent.

Severe types.—Malignant or " black measles," a very fatal toxic type in which hæmorrhages occur in the skin between the papules, and also in the mucous membranes, is excessively rare in this country. A severe toxic type which may be fatal from toxæmia quite apart from complications is still occasionally seen in persons bred in remote country districts, *e.g.* the West of Ireland or the Highlands of Scotland. In another rare toxic type, which may occur in infants, a shock syndrome with peripheral circulatory failure sets in before the rash is properly developed. A bullous form of the eruption (morbilli bullosi) occurs rarely and is very fatal; it must be distinguished from measles complicated by pemphigus (Ronaldson, 1937).

Complications

The most important complications are those of the respiratory tract. Catarrh of the bronchi is present in a large proportion of cases. In infants over six months this may lead to severe capillary bronchitis which may be fatal if not prevented or treated promptly by chemotherapy. *Broncho-pneumonia* is the most important and fatal complication. Its character and incidence vary in different epidemics. It is most frequent in infants aged from six months to one year and nearly as frequent at age one to two years. After two years its incidence rapidly diminishes, but it is always more apt to occur in young children with a previous history of bronchitis or pneumonia. In the more severe epidemics it is associated with interstitial infiltration and patchy atelectasis, and the worst cases may then show a heliotrope cyanosis similar to that seen in the influenza pandemic of 1918–19. This type has been found by lung puncture to be particularly associated with *H. influenzæ* infection of the lungs (Ellison, 1931). In milder epidemics the pneumonia is more lobular in type, with little interstitial involvement. In London, the incidence of clinical broncho-pneumonia has fallen considerably since 1934 and especially since 1940. Thus in the Park Hospital in 1933–4 its incidence was 13·8 per cent. of 1,290 cases; in 1935–6, 9·2 per cent. of 1,286 cases; in 1937–8, 10·5 per cent. of 798 cases and in 1943 with an approximately

similar age-grouping, 3·1 per cent. of 774 cases. The significant fall in incidence in 1943 was probably associated with prophylactic chemotherapy given to all cases on admission. From 1943 to 1951 a similar low incidence was consistently maintained. The fall in the fatality rate of hospital-treated measles since the advent of chemotherapy is even more striking than the fall in incidence of pneumonia.

Measles with broncho-pneumonia has frequently been the direct cause of chronic fibrosis of the lung or bronchiectasis which invalids a child for life. Since this disabling sequela seems to depend on the duration as well as the type of the broncho-pneumonia, and since chemotherapy in the broncho-pneumonia of measles has, so far, been rapidly effective it is to be anticipated that pulmonary fibrosis resulting from measles will be significantly reduced in future. The older belief that tuberculosis of the lungs is a frequent sequela of measles was probably largely due to confusion of tuberculosis with pulmonary fibrosis or bronchiectasis before the regular use of X-rays helped to sort out these conditions. The chief danger appears to be the production of miliary tuberculosis or tuberculous meningitis when an attack of measles and an active primary tuberculous complex coincide in time. The *laryngitis* of measles, if in young children and of severe degree, is always serious. The early form occurring in the prodromal stage may be accompanied by great œdema and ulceration of the larynx and tracheotomy at this stage has frequently in the past been fatal owing to development of broncho-pneumonia. The later form occurring after the rash has appeared has been, in hospital-treated cases at least, frequently due to secondary infection with diphtheria. If the diagnosis is in doubt diphtheria antitoxin should be given without delay. In order to prevent this serious complication it is well to give prophylactic diphtheria antitoxin on the admission to a measles ward of all young children who have not been immunized against diphtheria.

Alimentary tract.—Stomatitis occurs in (*a*) a catarrhal form with erythema and superficial pultaceous patches of exudate, (*b*) an ulcerative form in isolated patches, from trauma and secondary infection, or in diffuse small ulcers over buccal mucosa and tongue, a condition suggestive of incidental infection with the virus of herpes febrilis (primary herpetic fever), (Scott, 1941), and (*c*) an ulcerative gangrenous form, cancrum oris, which is now extremely rare, and is associated with poor nutrition, trauma and infection with anærobic bacilli. *Enteritis* with diarrhœa leading occasionally to dehydration is a serious complication in children under two years. It is usually combined with broncho-pneumonia, and appears to be much less frequent since the control of broncho-pneumonia by prophylactic chemotherapy. Suspicious symptoms of *appendicitis* may arise at about the height of the disease probably from catarrhal changes or lymphoid tissue enlargements in the neighbourhood of the appendix. Unless the indications are clear, operation should be deferred. It is surprising how often appendicectomy is unnecessarily performed in the prodromal stage of the exanthemata.

Suppurative otitis media, though much reduced in incidence since 1940, is probably still the most troublesome complication of measles.

In the Park Hospital series referred to above it occurred in 13·6 per cent. in 1933–4; 10·5 per cent. in 1937–8 and only 3·3 per cent. in 1943. As with broncho-pneumonia, a significant drop in incidence occurred when prophylactic chemotherapy was instituted (p. 1733). This, however, affects principally the otitis media of early onset, *e.g.* that occurring before the ninth day of the disease. After this stage, suppurative otitis media in hospital-treated measles is probably a ward cross-infection, like the late septic complications of scarlet fever. Thus, in measles, as in scarlet fever, a short period of isolation in hospital for uncomplicated measles is desirable. As soon as otitis media appears it should be vigorously treated with sulphathiazole or penicillin in the dosage for severe infections.

Eye complications include severe purulent conjunctivitis, blepharitis, dacryocystitis and corneal ulcer. Occasionally there is gross palpebral œdema, much purulent discharge, and even membranous exudate. The latter condition is usually due to a virulent strain of hæmolytic streptococcus, but the possibility of ocular diphtheria must be kept in mind (p. 1707). Unless recognized and treated at once, corneal ulcer may quickly lead to hypopyon or perforation. At best it leaves corneal opacities which interfere seriously with vision. Post-measles *encephalomyelitis* in its most common form does not differ clinically or pathologically, except in degree, from that complicating other infectious diseases of virus ætiology, *e.g.* smallpox, vaccinia, chicken-pox and rubella. In a high proportion of the cases following measles it is mild, the recovery rate being 75 to 90 per cent. There is a cerebral and a spinal type, which are often associated in the same case. The complication usually arises at the end of the first week when the rash is fading and the temperature has become normal. In the cerebral type, there is pyrexia, *drowsiness*, stupor or coma, muscular twitchings, signs of meningeal irritation, and there may be hemiplegia, hemiataxia or paralysis of various kinds. Pyramidal tract involvement is common; thalamic, hypothalamic and cerebellar signs are less frequent. In the spinal type the most characteristic symptom is paraplegia and loss of bladder control. The duration of symptoms varies greatly. Occasionally symptoms do not last more than two or three days and may be so mild as to pass almost unnoticed. Most cases are drowsy or unconscious for about a week, with or without various paralyses of the same or longer duration. Exceptionally a case occurs which runs a severe and prolonged course. I have records of one case completely comatose and paralysed for a month, which cleared up in about twelve months, with perfect recovery; and of another, comatose for over a week, who became permanently spastic, aphasic, and mentally defective. Excluding the 10 to 25 per cent. cases fatal within a week or two of onset, the prognosis is generally good and recovery appears in most cases to be progressive. Relapses, however, may occur and permanent mental and physical defect may be sequelæ. Parkinsonism is not a characteristic feature of this type of post-infective encephalitis. The characteristic pathological change found in fatal cases is a perivascular zone of lymphocytic and histiocytic cuffing in the first few days and, later, *demyelinization* with some damage to axis cylinders around many

of the small veins. The change is widely distributed in the white matter of brain and cord but grey areas, *e.g.* in hippocampus, basal ganglia, and nuclei of pons and cerebellum are sometimes involved. Significant damage is found in the ganglion cells, sometimes with neuronophagia. Appelbaum and his co-workers (1949) on the basis of seven autopsies considered the lesion to be primarily an inflammatory one. The fairly constant " incubation period " before the appearance of the rash is considered, on the other hand, to be in favour of a reaction of antigen-antibody type. During the acute stage the spinal fluid is usually under increased pressure, shows an increase of lymphocytes and monocytes, an increase in protein, and relatively normal chloride and sugar content. The incidence of measles encephalitis according to my own observation in cases admitted to hospital is about 1 per 1,000 cases. A rare form of encephalomyelitis appearing *before* the rash, has been described (Wyllie, 1934). It seems to be usually a hæmorrhagic encephalitis and quite different from the more common demyelinating encephalitis described above ; its prognosis may not be so good. As in other acute infections in young children, thrombosis of the superior longitudinal sinus is an occasional finding at autopsy.

Diagnosis

In the *prodromal or catarrhal stage*, the detection of the exceedingly minute Koplik's spots, their differentiation from other spots (p. 1724), and a history of exposure to measles some ten days previously distinguish measles from the common cold, influenza and the catarrhal stage of whooping-cough. In the *eruptive stage*, measles may be confused with rubella, scarlet fever, paratyphoid fever, smallpox, typhus fever, maculopapular drug, serum, enema and food rashes, papular urticaria and erythema multiforme of macular type. The rubella rash *appears* on the first or second day of symptoms, is pinkish, discrete and leaves no staining ; catarrh is slight and the post-cervical glands are considerably enlarged ; the spleen may be palpable ; Koplik's spots are never present. The *scarlet fever* rash, especially in septic cases, may be coarse, blotchy and almost morbilliform on the limbs, particularly on the extensor aspects. In *paratyphoid fever*, the long prodromal period and the absence of upper respiratory catarrh are significant features. *Smallpox*, both the minor and major varieties, has often been wrongly diagnosed as measles for a few days and generally with dire results. The rash of smallpox may remain papular for three days before the typical vesicles appear, especially in severe variola major. The typical catarrh of measles, the Koplik's spots or the later finely-granular uniformly reddened buccal mucous membrane would be absent, and the distribution of the smallpox rash would be quite different. *Typhus fever* is often mild and anomalous in children, but the rash does not appear till the fifth day of disease or later and is *not present on the face*. *Sulphonamide rash* with or without fever is often morbilliform, but other signs of measles are absent. Salicylates, belladonna, or veronal, may also give rise to morbilliform rashes. Serum rashes may be partly morbilliform but nearly always have an urticarial element.

The *post-measles staining stage*, when vivid and purplish, has frequently been misdiagnosed as typhus, hæmorrhagic smallpox, and meningococcal septicæmia.

Prognosis

This depends mainly on (1) the character of the epidemic, particularly as regards the occurrence of the interstitial type of pneumonia, (2) environmental hygiene, (3) the age (see p. 1723), and (4) the nutritional state of the patient. Particularly serious is the active form of rickets so liable to be associated with pulmonary and intestinal complications, and still to be seen in northern industrial districts. Fatality has been as high as 40 per cent. in some epidemics. Chemotherapy has in the last few years greatly lowered fatality and probably also the damage from chronic pulmonary fibrosis, otorrhœa and corneal opacity. In 1931–2, out of 11,526 cases admitted to the London fever hospitals, the death-rate was 5·6 per cent., in 1942 out of 4,354 cases so admitted it was only 0·38 per cent. and it has since remained at about this figure. Laryngitis, convulsions, diarrhœa and vomiting in infants are now often more serious than pneumonia. Association of acute measles with the acute stages of other infectious diseases, particularly diphtheria and whooping-cough, is always serious.

Treatment

Diet should be as generous as the child's febrile state permits; milk, milk foods, jellies, during the pyrexial stage; minced meat, fish, green vegetable and fruit as soon as the temperature has dropped. Under-nourishment must be avoided as far as possible from onset. The patient must be warm and dry, and good ventilation and air space maintained, whether at home or in hospital wards. In epidemics, the temptation to reduce bed-spacing below 10 to 12 feet between cot centres must be resisted. Regular nursing toilet of the mouth, lips and eyes, is comforting and preventive of secondary infection. Laryngitis is treated by the steam tent and hot applications to neck and chest, and if distressful by chloramphenicol and tracheotomy. Laryngitis arising after the rash should be treated as diphtheritic, unless there is proof to the contrary. For bronchitis, the steam tent is useful in the dry stage. Opiates are usually undesirable; they may tend to retention of secretions and production of pneumonia. In established pneumonia, sulphathiazole, sulphadiazine, and sulphadimidine are, with penicillin, the best available drugs. The oxygen tent is of great adjuvant value in pneumonia in infants. When broncho-pneumonia is prolonged for two weeks or more, there is always some residual pulmonary fibrosis. A special effort should be made to give such children a prolonged period of hygienic open-air treatment on ward verandahs. If possible they should be so treated throughout the summer following their attack. Most of these patients, being under three years of age, are not catered for in convalescent homes. They should, however, be followed up, with X-ray of chest at frequent intervals. When enteritis develops in children under two years they

must be separated from others of this age. In purulent conjunctivitis penicillin or aureomycin is usually rapidly effective. In severe cases with or without corneal ulcer, irrigations two-hourly or more often may be necessary for a day or two. Atropine (1 per cent. drops daily) to keep the pupil well dilated is indicated in corneal ulcer. The causal organism should be investigated for penicillin and sulphathiazole and other antibiotic sensitivity.

General prophylaxis

Notification of measles was made compulsory in October 1939. *Isolation* of the patient is desirable for about ten days from onset, but infectivity is highest during the catarrhal and early eruptive stage and ceases, even in complicated cases, about four days after the rash appears. Uncomplicated cases in hospital are best discharged after about ten to twelve days residence. Exclusion of contacts, other than infants, from school has not been found to be effective in lowering the incidence of measles and is not now practised in London. If *quarantine* is imposed upon contacts who have not had measles, the period is normally fourteen days from the date of appearance of the rash in the last case, but this should be extended to at least twenty-one days for contacts who have had prophylactic serum. *Hospitalization* of measles in the eruptive stage has little or no effect on incidence. Hospital treatment can, however, be highly effective as a public health measure in preventing mortality and morbidity, especially from pulmonary, ear and eye complications.

Sero-prophylaxis.—Human serum must be used; no animal serum is of any value. There is no serum-therapy in measles, since by the time symptoms appear, the serum is ineffective against the virus (cf. poliomyelitis serum) even when used in large doses intravenously. Serum is used only for *non-immune contacts* in order to prevent or attenuate the disease. It is a most useful measure in hospital contacts, where isolation of the primary case is practised. It is also useful for home contacts in small families, but may not be fully effective in homes where the immunized child is repeatedly exposed to an infected brother or sister.

Nicolle and Conseil (1918) are generally credited with being the first to use convalescent serum in the epidemiological control of the disease. They showed that specific antibodies are present in the blood in high concentration about a week after the acute stage of measles and thereafter remain throughout life in somewhat diminished potency. *Convalescent serum* taken from the patient about the tenth to the fourteenth day of the disease, and injected in doses of 5 to 10 c.cm. intramuscularly into contacts under five years of age during the first five days after exposure to infection, will usually protect completely against measles (*sero-prevention*). The same dose given from the sixth to the ninth day of exposure will usually modify the disease (*sero-attenuation*). The latter object, however, can be more economically obtained, by injecting half the dose (2·5 to 5 c.cm.) during the first five days after exposure. The advantage of sero-attenuation is that the child has a mild and harmless attack of the disease and is, as far as we know,

thereafter immune. When sero-prevention is successful, the immunity is passive and lasts only for three weeks, after which the child is as susceptible to measles as before.

In practice, a supply of convalescent serum is difficult to maintain. Accordingly, *adult serum* is frequently used for the prophylaxis of measles. Donors should be persons who give a history of measles within the past twenty or thirty years. There is at present no method of measuring its anti-measles potency. It is, however, generally reliable for producing sero-attenuation of satisfactory degree, if injected intramuscularly into contacts during the first five days after exposure to infection, in about double or treble the dosage used for convalescent serum, *i.e.* 10 to 30 c.cm. in children under five years. Adult serum cannot be relied upon for sero-prevention. When children of varying ages are being injected with adult serum, a useful rule is to give a dose of (age $\times$ 4) c.cm. with a minimum of 10 c.cm. and a maximum of 20 c.cm. up to five years. Sero-attenuation is rarely practised in contacts over the age of five years, but if so, 30 c.cm. should be given. In the preparation of both these sera, the blood is collected aseptically in agar-lined bottles, thus ensuring a high yield of serum. The serum is tested by the Wassermann reaction, filtered through a Seitz filter to ensure sterility, and ampouled at once with 0·5 per cent. phenol or with merthiolate. Alternatively it may be dried until required. Ampouled serum kept in the cold room maintains its potency for about six months. Dried serum remains potent indefinitely. *Convalescent serum*, when injected into the rash of measles, is unable to blanch it, but when it is given a few days before the rash appears, the rash may not develop at the site of injection and so a blanched area is produced (phenomenon of Debré).

Adult blood is sometimes used as a substitute for serum in the prophylaxis of measles, *e.g.* by injection of 30 to 40 c.cm. blood from a parent intramuscularly into a child, within five days of exposure to infection. This may produce some degree of attenuation, but a disadvantage is the large hæmatoma with its liability to secondary infection and severe sloughing.

Placental extract (immune globulin) was first prepared as a substitute for serum in the prophylaxis of measles by McKhann and Chu (1933). It is an extract of human placentæ containing globulins, to which are attached those immune bodies present in adult serum that are capable of passing the placental barrier. The dosage is said to be low, *e.g.* 2 to 4 c.cm., but the potency cannot be accurately assessed, and probably 5 to 10 c.cm. is nearer the effective dose. A disadvantage is a tendency to local and general reactions. It is now rarely used.

The use of human serum cannot be said to be devoid of the risk of causing serum hepatitis after an incubation period of approximately ninety days. The cause is probably a virus present in the presumed healthy subject at the time of collection of the blood. The risk in the use of human serum is, however, small provided that large pools of serum are avoided. In the fever hospitals in London, many thousands of doses of convalescent and adult human serum were injected for the prophylaxis

of measles during the years 1930–45 without a single authenticated case of jaundice arising so far as is known. This serum was mostly prepared from single donors. If pooled serum only is available the risk may be such as to contra-indicate this method of prophylaxis.

Gamma globulin.—Fractionation of human plasma by electrophoresis, that is the process by which the different protein molecules of the plasma move at different speeds when submitted to an electric field, separates the albumin, alpha and beta globulins, fibrinogen and gamma globulin (Cohn and others, 1944). The gamma globulin amounts to 11 per cent. of the total and is the fraction which contains most of the immune bodies. In its final state it represents a twenty-five-fold concentration of the gamma globulin of the original plasma. It can be heated at 57° C. for four hours, without significant change, and it has been claimed, though not yet conclusively proved, that this degree of heating destroys the virus of infective hepatitis. Among 3,000 children injected, Stokes and others (1948) could find no case of serum hepatitis. In the prophylaxis of measles in contacts it has given brilliant results, being more than twice as potent, volume for volume, as convalescent serum and placental extract (Greenberg and others, 1944). Dosage is not yet finally settled, but almost complete protection has been obtained with 0·1 c.cm. per lb. of body-weight given up to the fifth day from exposure and about half this dosage is used for attenuation. A subcommittee reporting to the Medical Research Council (1948) found that the volume of Cohn's gamma globulin required for the prevention and attenuation of measles was about half the dose of convalescent measles serum. This is now the method used in London.

Chemoprophylaxis.—Sulphonamide prophylaxis of complications of measles appears to have been strikingly effective in reducing the mortality and morbidity of the disease. The drug is conveniently administered from the fourth or fifth day of the disease, when the rash is well out. This is the period when the virus phase of the disease begins to decline and the bacterial phase to advance. Sulphathiazole, sulphadiazine or sulphadimidine given for five or six days from the appearance of the rash is nearly always effective in preventing the onset of broncho-pneumonia, otitis media or severe ophthalmia during the period of its administration and a day or two thereafter. The dosage required is not high, *e.g.* 0·5 gramme six-hourly under five years. Such chemo-prophylaxis, supplemented by chemotherapy for complications present on admission, was associated with a reduction in the case fatality rate in the Park Hospital for the four years 1940–3 to about one-tenth of what it had been in previous epidemics. Broncho-pneumonia and otitis media were greatly reduced in incidence and occurred mainly after the ninth day of disease when the effect of the chemoprophylaxis was withdrawn. As in scarlet fever, however, these late septic complications, due to ward infections in hospital-treated cases, may often be avoided by restricting the isolation period to ten or twelve days. In hospital practice it is desirable to combine chemoprophylaxis with an injection of 1,000 to 2,000 units of diphtheria antitoxin on admission, so as to prevent the risk of secondary infection with diphtheria in non-immunized patients.

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WHOOPING COUGH

Synonyms.—Pertussis and parapertussis, *Fr.* Coqueluche, *Ger.* Keuchhusten, *Ital.* Pertosse, tosse ferina, *Span.* Tos ferina.

Definition.—Whooping-cough is a specific infectious disease caused by the bacillus of Bordet-Gengou (*Hæmophilus pertussis*) or an allied organism (*Hæmophilus parapertussis*) and characterized by tracheal and bronchial catarrh, paroxysms of coughing and usually long-drawn inspirations or "whoops."

Epidemiology.—Pertussis is endemic in most centres of population in temperate climates. In the larger towns epidemics tend to occur biennally, alternating with measles. In less populous places, periodicity is less regular or spaced at longer intervals, *e.g.* four to five years in Denmark. The main *seasonal* incidence is in spring, but this is far from being constant. An epidemic may continue throughout the summer and last as long as a year. Stocks (1932) concluded from a statistical study of London epidemics that an epidemic wave is brought to an end through the latent immunization of contacts. The immunity so gained is temporary and lapses within a year. This brings about a sharp increase of susceptibles and the conditions for another outbreak about twelve months after the first has ended.

Sex incidence.—There is a regular slight preponderance of females, an unexplained phenomenon.

Age.—It is pre-eminently a disease of infants and the youngest children. There is little or no immunity transmitted from mother to offspring as in measles, diphtheria and scarlet fever. Newly-born babies are usually susceptible to the disease and should always be specially protected from it, since the highest case fatality rate occurs in the age period under three

months. Zamkin (1940) showed in one study that 10·5 per cent. of all cases and 40 per cent. *of all deaths* occurred in the first year of life. This trend has since been accentuated. More than two-thirds of the deaths occur under the age of one year, and more than half of these take place in the first six months (Min. of Health, 1949). Between 80 and 90 per cent. of the cases occur from one to five years. After this age, the disease is uncommon and fatality negligible. In a study of 7,481 schoolboys aged thirteen to eighteen years (M.R.C. Report, 1938), it was found that over 70 per cent. had had both measles and pertussis. Yet adults who have escaped the disease are not permanently immune and are liable to take it at any age, often in atypical form without the whoop. A single attack usually confers lasting immunity, although second attacks are known to occur.

Whooping-cough was made a notifiable disease in Britain in October, 1939. In 1941, a year of high prevalence, 173,331 cases were notified in England and Wales, and there were 2,383 deaths, a figure approximating to the diphtheria deaths for the year. This gave a general fatality rate based on notifications of about 1·25 per cent. The corresponding figures in 1948, however, were 146,383 notifications and 748 deaths, a drop in general case-fatality to 0·51 per cent. This improvement must be attributed mainly to penicillin treatment. The fatality rate among 2,000 or more cases treated in the London County Council fever hospitals annually from 1933 to 1937 varied from 7 to 10 per cent. For the period 1939–42 the corresponding case fatality rate dropped to between 3·0 and 3·5 per cent., a sudden reduction synchronizing with the sulphonamide treatment of broncho-pneumonia. The reduction of the case fatality rate for whooping-cough since 1939 is not, however, nearly so great as the corresponding reduction for measles. The permanent morbidity is no less serious than the mortality. There is still a considerable incidence of crippling complications and sequelæ, especially bronchitis, broncho-pneumonia, lung collapse and bronchiectasis.

Bacteriology.—There is overwhelming evidence that the cause of the disease is not a filterable virus but the small gram-negative cocco-bacillus *H. pertussis* or a closely allied organism *H. parapertussis*. *H. pertussis* can be cultured from over 90 per cent. of patients in the first week of the disease, and from a diminishing proportion thereafter till the end of the fourth week (Sauer, 1938; Silverthorne and Fraser, 1935; Donald, 1938). It is rarely cultured from convalescents and hardly ever from unaffected persons. With cultures the disease has been reproduced in susceptible human volunteers and not in immunized controls (MacDonald and MacDonald, 1933); this has not been achieved with culture filtrates. Specific anti-bodies to *H. pertussis* can be detected in the blood of patients by agglutination and complement fixation from about the end of the third week of the disease until about the twelfth week (Kendrick, Gibbs and Sprick, 1937; Mishulow *et al.* 1942).

H. pertussis grows abundantly on the ciliated epithelium of the trachea and bronchi during the first weeks of the disease. A local reaction to this growth is the production of thick tenacious mucus. The spasmodic

cough is probably a protective reflex mechanism developed by the body to get rid of this mucus. The organism is cultured from the mucus by means of cough plates or per-nasal swabs (p. 1740) on special Bordet-Gengou agar medium containing 50 per cent. of blood together with extract of potato and glycerine. The isolation of the organism is greatly facilitated by the addition of penicillin to the medium as an inhibitor of organisms other than *H. pertussis* (Fleming, 1929; Cruickshank, 1944). On this medium the tiny mercury-drop or pearl-like colonies of the organisms are looked for after *three days incubation*, suspected colonies being picked off and tested by slide agglutination.

Leslie and Gardner (1931) showed by agglutination methods that *H. pertussis* is capable of undergoing dissociation into four serological variants which they termed phases I, II, III, and IV. Phase I is the form recovered in the primary cultures from cases of whooping-cough, and the other phases are liable to develop in subcultures. Phase I organisms are always hæmolytic, possess a capsule and contain about ten times more toxin than those of the other phases. Phase I is the virulent or " smooth " form of the bacillus, while phases II, III and IV are " rough " non-virulent forms. The importance of this is that if any prophylactic vaccine is to be of value it must be made from phase I cultures, and not from organisms frequently subcultured in the laboratory.

H. parapertussis, first isolated from cases of whooping-cough by Eldering and Kendrick (1937), grows more luxuriantly and with darker colouration than *H. pertussis* in sub-culture on Bordet's medium, and can be differentiated from it by agglutination and absorption methods. It has been cultured in certain areas from children with mild whooping-cough or with slightly suspicious coughs. It seems to be very rare in London. There is some evidence that there is little cross-immunity between these organisms.

Immunology.—The immunological mechanism responsible for the permanence of immunity following an attack of whooping-cough is not fully understood. It does not seem to be due to permanent circulating humoral antibodies. The *bacterial antibodies* in the blood of patients, as shown by the complement fixation and other tests, disappear after the twelfth and fifteenth week of the disease. Pertussis *antitoxin* production in human beings is irregular and weak and is confined to the active phase of the disease. Antitoxin has not so far been demonstrated in the blood in the convalescent stage (Weichsel *et al.*, 1942; Bullowa *et al.*, 1942). It has been suggested that permanent immunity may be due to local tissue immunity in the respiratory tract, but of this there is no proof.

Symptomatology.—The onset is always gradual following an incubation period of five to fourteen days. The disease starts like an attack of bronchitis with slight fever and a cough which becomes progressively worse especially at night (catarrhal stage). The cough soon becomes paroxysmal in character, the spasms are more prolonged, occurring at shorter intervals, and are finally associated with a whoop in typical cases (spasmodic stage). Vomiting after a fit of coughing is such a common feature that a presumptive diagnosis may sometimes be made before the

confirmatory whoop appears. In infants under three months, spasm of the glottis during a paroxysm prevents the whoop and dangerous apnœa may frequently occur and lead to convulsions or asphyxia. In many abortive cases, especially in older children and adults, paroxysms are short and there is no whoop. Paroxysmal sneezing occasionally replaces the cough.

Once the cough has been heard it is not easily forgotten, and subsequent cases can usually be diagnosed by ear alone. The child gives a series of about ten to twenty short, forceful coughs, during which inspiration is temporarily suspended. The face turns purple, the veins of the face and scalp stand out, the tongue is protruded and the eyes water and bulge forward. At the critical moment when asphyxia seems imminent, a long drawn inspiratory crow or whoop comes to the rescue, but it is immediately succeeded by another fit of coughing followed by a whoop. This is repeated five or six times, and with the final effort a mass of tenacious mucus is expectorated and the child vomits. The vomiting may recur so frequently that the child retains little food and wastes rapidly. The number of paroxysms varies. In mild cases, there may be no more than five or six during the twenty-four hours ; in severe attacks a paroxysm may occur about every half-hour. The spasms may arise spontaneously or be stimulated by excitement, emotions such as anger, fear or laughter or by taking food. In young children the sputum is usually blood-streaked, and fæces and urine are voided during the spasm. When the spasm is over, the child falls back exhausted, breathing rapidly, sweating and sometimes mentally confused. Older children are much less affected in these ways. Severe spasms unaccompanied by good whooping tend to lead to broncho-pneumonia, possibly because of the patchy atelectasis which is first produced in such cases. Conversely good strong whoops appear to be some protection against broncho-pneumonia. In severe broncho-pneumonia with feeble general condition, the spasmodic cough and whoop may be far from characteristic or may even be absent. The spasmodic stage varies from three weeks in mild cases to several months in severe attacks occurring during the winter. It sometimes persists for many months as a habit with subconscious motivation.

Physical signs.—The mechanical strain on the circulation causes the face to become bloated. Œdema under the eyes may suggest nephritis, but the typical pallor of the latter condition is absent. Signs in the chest are not conspicuous during the catarrhal and early spasmodic stages. A few sticky râles and numerous rhonchi, sometimes with diminished or bronchial breath sounds over collapsed areas, are often present in the later stages. X-ray films of the chest even in uncomplicated cases about the third and fourth weeks frequently show peri-mediastinal and infra-hilar triangular shadows (Debré *et al.*, 1938 ; Maggi, 1941). X-ray screening during a spasm frequently reveals atelectatic portions of the lungs.

The blood picture.—There is a well-marked relative and absolute lymphocytosis in the late catarrhal and spasmodic stages. This is sometimes present also in the early catarrhal stage and even in the incubation period, but occasionally leucopenia is found at this early period. The

lymphocytosis has been known to be as high as 230,000 per c.mm. returning to normal with the subsidence of the disease. The lymphocytosis is a useful diagnostic feature sometimes present as early as the first week; but the normal lymphocytosis of young children must be taken into account. Under the age of three years, a white cell count to be significant for diagnosis should be over 15,000 per c.mm. with 60 to 80 per cent. lymphocytes and associated with a suspicious cough.

Complications and sequelæ.—*Localized hæmorrhages* may occur, due to the passive congestion during the paroxysms sometimes combined with hæmatological or nutritional abnormalities. *Sub-conjunctival* hæmorrhage, the most common form, was much more frequent thirty or more years ago than it is to-day. Minute petechiæ about the neck, shoulders and upper chest are not uncommon. I have found one or more symptomless retinal hæmorrhages in each eye during fundus examination. True *hæmoptysis*, hæmatemesis and hæmorrhage from the tympanic membrane are very rare. Multiple capillary or larger *cerebral hæmorrhages*, and also meningeal hæmorrhages, are rare causes of death. Other complications due to the mechanical strain of the paroxysms are umbilical and inguinal *hernia, prolapse of the rectum, interstitial and subcutaneous emphysema* and *pneumothorax*; those due to friction trauma are ulcer of the frænum of the tongue, and of the buccal mucosa opposite the teeth.

Respiratory complications.—The most fatal complication of pertussis is broncho-pneumonia. It may occur at any stage, frequently as late as three or four weeks after onset. The causal organisms are not determined with certainty except by lung puncture, which is now generally regarded as unjustifiable. A per-nasal or laryngeal swab, however, often gives a clue. Pneumococci and hæmolytic streptocci are probably the most frequent causal organisms although the broncho-pneumonia of pertussis responds less rapidly than that of measles to sulphonamides and penicillin. Physical signs are often ill-marked and difficult to interpret since *patchy atelectasis frequently accompanies the broncho-pneumonia in infants.* Resolution in cases which fail to respond to sulphonamides rapidly tends to be slow and irregular, and to leave behind a variable amount of pulmonary catarrh, bronchiolitis or fibrosis which may ultimately result in bronchiectasis. Routine X-ray examination of the chest in whooping-cough reveals atelectasis of the lower zone present in a surprising number of cases, even afebrile cases without pneumonia. Generally it shows as small patches of shadow, in the cardio-phrenic angles, corresponding to acinar or segmental collapse, but sometimes the whole lower lobe, middle lobe or linguala is collapsed. On the left side the line of the collapsed lower lobe may be seen running obliquely through the heart shadow. Lateral or oblique skiagrams are usually necessary for diagnosis of the area of collapse. In a fair number of cases the collapse does not clear up and still shows in the X-ray film a year or more after the acute stage. In the ætiology of bronchiectasis in children much more attention should be paid to whooping-cough than is now the case.

Gastro-enteritis tends to occur as a complication in young infants (secondary gastro-enteritis), but in hospital cases it is not infrequently

due to cross-infection either with known pathogens, *e.g.* Sonne dysentery or with the much more serious non-specific variety.

Albuminuria of a transient kind is not uncommon. True nephritis is rare and likely to be associated with secondary streptococcal infection. Temporary glycosuria has been described, possibly associated with cerebral hæmorrhage.

Nervous complications.—*Convulsions* rank next to broncho-pneumonia as a cause of fatality. They may occur either at the end of or between paroxysms, and may or may not be associated with broncho-pneumonia and atelectasis. They may be single or repeated so frequently as to constitute a *status epilepticus*. They are usually generalized but may be localized to the face or a limb. They are most frequent and severe in rachitic infants with low serum calcium, but are by no means confined to these. Their cause is uncertain. They have been attributed to the action of a neurotoxin, to cerebral anoxæmia or ischæmia due to vasospasm, to air embolism and to encephalitis. The single convulsion occurring with a paroxysm is most likely to be due to anoxæmia.

Pathological changes which have been found in the brain consist of œdema, ischæmic cellular degeneration, multiple microscopic hæmorrhages and lymphocytic plugs in veins and capillaries. These suggest a circulatory disturbance rather than a toxic effect on the nervous tissue. These lesions are sometimes associated with tissue repair changes which may be interpreted as a secondary encephalitic reaction. Other nervous complications which may be due to similar causes are *hemiplegia*, *paralyses* of upper neuron type associated with drowsiness and pyrexia, *aphasia*, *blindness* and *deafness*. The paralyses usually clear up in a few weeks. Blindness has also arisen from detachment of the retina.

Otitis media is not very frequent and is usually due to secondary streptococcal infection. Mastoiditis in whooping-cough is quite rare.

Associated infections.—Since the victims of pertussis are usually very young they are liable to contract other infections concurrently, *e.g.* measles, gastro-enteritis, diphtheria or scarlet fever. Double infections of this nature are particularly serious and all possible steps should be taken to prevent or mitigate them, *e.g.* sero-prophylaxis of measles. Miliary tuberculosis occasionally supervenes in young children, probably when a concurrent active primary complex is present. Hilar and bronchial gland tuberculosis may also be stirred into activity, but this is rarer than was formerly believed. The chronic pulmonary sequelæ are much more frequently of bronchiectatic than of tuberculous type.

Psychopathic sequelæ.—Lurie and Levy (1942) suggested that certain neurological findings and behaviour disorders in "problem" children might be traced back to an attack of whooping-cough. These included pyramidal and extra-pyramidal lesions, nerve deafness, speech disorders, abnormal electroencephalograms, emotional weakness, progressive intellectual deterioration, and post-encephalitic type of hyperactivity and destructiveness. No real evidence, however, that these changes were in fact due to whooping-cough has been produced.

Diagnosis.—Early diagnosis is essential to the control of the infection.

This is not easy before the whoop appears. A history of exposure to infection, a spasmodic cough, especially if followed by vomiting, a leucocytosis of 12,000 or more with over 60 per cent. of lymphocytes, and a normal erythrocyte sedimentation rate, taken together make the diagnosis almost certain.

Laboratory methods include the cough-plate and the per-nasal swab.

Cough-plate method.—The child is given a drink of water to clear the mouth of extraneous organisms. A paroxysm is induced by movement of the cricoid upwards and downwards ; or by extension followed by sharp flexion of the head of the child while the thumb of the operator is held in the supra-sternal notch riding lightly over the child's trachea during flexion of the head. Two Petri plates containing Bordet-Gengou medium are held about four inches in front of the mouth during the paroxysm while each plate receives the spray from three or four good coughs.

Per-nasal swab.—This is made from seven inches of fine Nichrome wire (S.W.G. 25), the last quarter of an inch being bent back to form a lodgment for a thin wisp of cotton wool. After a paroxysm has been induced by one of the methods indicated above, the swab is passed gently along the floor of the nose to the posterior wall of the naso-pharynx. (Cockburn and Holt, 1948). With modern technique both these methods are of high but not absolute value in diagnosis. In the first two weeks of the disease at least 80 per cent. of cases may be diagnosed by one or other or both of these methods.

Skin tests.—These have, so far, been quite unreliable. One reason for this may be that the reagents employed have contained antigens producing both a sensitivity and an immunity reaction. Flosdorf's agglutinogen (Flosdorf and his colleagues, 1943) has been claimed to produce a pure sensitivity reaction, but in controlled trials in Park Hospital this antigen gave quite unreliable results.

Paroxysmal cough may also be produced by influenza, enlarged tonsils and adenoids, and by enlargement of the bronchial glands, but in these disorders paroxysms are usually short and there is no whoop. Bronchial asthma and laryngismus stridulus may give rise to difficulty. In the former respirations are wheezy and there is eosinophilia ; in the latter, there is no spasmodic cough.

Prognosis depends on the age and on the nutritional status of the child. The younger the infant, the worse the prognosis. Under three months, fatality is very high. Convulsions, broncho-pneumonia and diarrhœa in that order greatly worsen the prognosis—and these complications are more prone to occur in children with active rickets than in normal children. Atelectasis affects the remote prognosis.

Treatment.—Children with uncomplicated whooping-cough should be allowed to run about in the fresh air, adequately protected from the cold. This is better than confining them to bed and is an advantage of home over hospital treatment. The practical difficulty is to isolate a child from susceptibles during the long period of infectivity of four or five weeks. This is especially important where there is a newly-born or very young

infant in the house. In such case the infected older child should always be sent away before contact is established with the young infant. If this is impossible the infant should be kept covered with muslin and an attempt made at passive immunization with gamma globulin or even active immunization with vaccines. If a child must be kept in bed he should be in fresh air protected from draughts. For an infant under three months an oxygen tent during the height of the paroxysmal stage is desirable, even in uncomplicated cases. It reduces the number and severity of the spasms. It is still more necessary if broncho-pneumonia supervenes. The maintenance of nutrition may be difficult owing to vomiting after the paroxysms. It is often necessary to arrange for feeding after paroxysms, so that the food may be retained. Milk should be given in small quantities at frequent intervals. Solid food should be finely divided and should not be dry or crumbly in order not to excite coughing. In infants, any symptom of gastro-enteritis should be treated at once and the child isolated. During a paroxysm all children should be trained to use a basin for their expectoration ; their backs should be supported and they should be reassured and comforted. The lips should be wiped with damp cotton wool swabs kept at hand in a container beside the basin.

Pertussis vaccines, toxoid or other extracts, and all forms of serum therapy are useless for treatment in the paroxysmal stage. Drug treatment is symptomatic and palliative ; it is unreliable for diminishing the frequency and severity of the paroxysms. Temporary relief may sometimes be obtained from belladonna, 10 to 15 minims of the tincture according to age, three times daily ; signs of intolerance may appear with this dosage. Ephredine $\frac{1}{12}$ grain for an infant to $\frac{1}{2}$ grain for a child of five years, three times daily, relaxes the bronchial muscle and may be combined with belladonna. Phenobarbitone is sometimes useful where spasms are severe and prolonged, in doses of $\frac{1}{24}$ grain for an infant, $\frac{1}{6}$ grain for a child of two years and $\frac{1}{3}$ grain for a child of five years, three times daily. Vitamin C is indicated as for normal children. There is no proof that a large surplus has any effect on the spasms. Similarly, ultra-violet light is beneficial to many young children whether afflicted with whooping-cough or not, but cannot be relied upon to modify the disease. The same may be said for X-ray therapy. Routine sedative drugging, *e.g.* with a linctus of codeine and belladonna, to relieve the spasms of whooping-cough is not to be encouraged. More harm than good may be done by suppressing whooping, since patchy collapse and broncho-pneumonia may then more readily supervene. Cod-liver oil and iron are frequently indicated in convalescence. Inhalations of vapour medicated with a crystal of menthol may occasionally be found useful in the catarrhal stage. Vaporization of creosote by means of a lamp sometimes has a striking effect, possibly psychological, in alleviating paroxysms at night and so promoting sleep. High flying and low pressure atmospheres appear to exert a striking curative effect in about 25 per cent. of uncomplicated cases from the third week onwards. Any acute respiratory inflammation or cyanosis contra-indicates this treatment (Baldry and Richou, 1946). In Park Hospital decompression treatment lasting ninety minutes at a pressure

equivalent to that of a height of 12,000 feet was given during 1949–51 to 500 children and adults, with results similar to those indicated.

Chemotherapy. Of the various antibiotics tried chloramphenicol (chloromycetin) in the writer's experience is probably the best. The daily dose is 60 to 120 mgm. per kgm. body weight in three or four divided doses. The course should last for at least ten days, since, with a shorter course there is a tendency to relapse and for *H. pertussis* to re-appear in cultures. During the treatment *H. pertussis* disappears but its growth is only inhibited. If treatment can be carried on until the end of the third week of the disease, the rising immunity will in most cases prevent a recurrence. This drug is also of great value in broncho-pneumonia complicating whooping-cough, especially those cases which fail to respond rapidly to penicillin.

Hyperimmune human serum.—This is not available in Britain but has been extensively used in the United States. On the basis of an experience of eight cases treated within the first two weeks of the disease, the writer considers that it may be effective in limiting the course of the disease in infants under six months of age. Four doses of the equivalent of 20 c.cm. human serum at daily intervals are required. Both these remedies appear to have a specific action, but like all other remedies in whooping-cough their effect is seldom dramatic.

Broncho-pneumonia is routinely treated by sulphathiazole or sulphadiazine ½ gramme four-hourly up to three years of age and by penicillin in large doses, at least 100,000 units three-hourly. The oxygen tent or oxygen by nasal catheter are valuable auxiliaries. It does not respond, however, so rapidly as the broncho-pneumonia of measles. This may be due to causal organisms, insensitive to the drugs, *e.g. H. pfeiffer* or *H. pertussis*, or to the patchy areas of collapse which commonly complicate the pneumonia. The oxygen tent among other actions reduces the number of spasms and gives rest. Sometimes an oxygen tent is required for as long as three or four weeks. Cases of prolonged broncho-pneumonia (over ten days pyrexia) require special care and the best of hygiene for many months in convalescence in order to minimize the residual lung damage. Serial X-ray films of good quality are necessary to check the condition of the lungs. Breathing exercises, and in young non-co-operative children, inhalations of oxygen and 7 per cent. CO_2 are useful in convalescence. Cases showing persistent areas of collapse in the lower lobes should have postural drainage by means of the Brompton frame. They must be followed up for several months or until skiagrams show complete re-expansion. An experience of bronchoscopy and suction in some twenty cases in Park Hospital was not a conspicuous success.

Convulsions are treated by warmth and lumbar puncture, and, if combined with broncho-pneumonia, the oxygen tent. The status epilepticus is, nevertheless, often fatal. Attempts may be made to control it by phemitone or by phenobarbitone soluble 1 grain in sterile solution intramuscularly for a child of five years, repeated as required.

Epanutin (1 capsule daily for a child of five) raises the threshold of electrically induced convulsions, and might be tried in this desperate

condition. Paraldehyde per rectum or intravenously is one of the best remedies. Pentothal sodium 0·05 to 0·1 gramme intravenously has been known to stop convulsions. If there is evidence of active rickets, 5 to 10 c.cm. calcium gluconate 10 per cent. solution should be injected intramuscularly, followed by calciferol by mouth or irradiation with ultraviolet light.

Prophylaxis.—*Isolation* is most effective when applied from the catarrhal stage onwards and should be for four weeks from onset of the spasmodic cough. Many children whoop and even vomit long after this period, but the cough-plate method has shown that infectivity practically ceases after four weeks. *Quarantine* of *school* contacts is now applied only to those in the Infant Department and for a period of 21 days. Disinfection of articles soiled by the patient during the illness and spring cleaning of room and furniture at the end of it is sufficient. *Passive immunization* of contacts by convalescent serum (taken in the eighth week of the disease) or by adult serum or blood or gamma globulin cannot yet be said to be of *proved* value. Fothergill and Walker (1939) were unable to demonstrate any difference in the bactericidal activity of convalescent blood as compared with blood from non-immune patients.

In recent years several different pertussis antitoxins and anti-bacterial sera have been prepared from horse and rabbit blood. A concentrated anti-toxic and anti-bacterial pertussis serum made in Britain, and which showed considerable activity against infection in mice, was tried in 1946 in several London Hospitals, including Park Hospital. No apparent success in the prophylaxis or treatment of the disease was observed. Indeed, several contacts who were injected with this serum developed the disease.

Active immunization by vaccines is the main hope of the future, but in this field also, claims of success are conflicting. The difficulty is to obtain a sufficiently potent pertussis antigen. The vaccine must be made from *phase I* strains which have been proved by complement fixation, agglutination or mouse protection tests to be capable of producing antibodies ; injections should be spaced at intervals of three or four weeks. A course of three doses is given at any age from two months onwards, followed by a boosting dose after one to two years. The Medical Research Council controlled trials showed attack rates of 18·2 per cent. in the inoculated and 87·3 per cent. in the uninoculated groups. Prophylactic vaccine may and should be used in individual cases with a fair prospect of mitigating if not altogether preventing the disease. In Canada and many parts of the United States results of vaccine prophylaxis appear to be satisfactory. A fluid vaccine combined with diphtheria and tetanus toxoids appears to have given good results in Canada. This can be given subcutaneously without much reaction. Subcutaneous injection is probably safest during periods of prevalence of poliomyelitis, since, in England, immunization by the intra-muscular route against diphtheria or whooping-cough has been attended by a number of cases of paralysis of the inoculated arm. Martin (1950) first showed that these must be regarded as cases of post-inoculation poliomyelitis.

Byers and Moll (1948) reported fifteen cases of *encephalopathy* immediately following injection of pertussis vaccine. These were collected over a period of ten years, and represent a minute fraction of the hundreds of thousands of children inoculated during the period. In most cases convulsions occurred within twenty minutes to seventy-two hours after the injection. Serious sequelæ including palsies, recurrent convulsions and progressive dementia resulted in some of the cases. It has been suggested that in such cases the inoculation may act merely as a " trigger mechanism " in convulsion-labile children.

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CHICKEN-POX

Synonyms.—Varicella, Glass-pox. *Fr.* Varicelle, *Ger.* Varizellen, Windpocken, Spitzblettern.

Epidemiology.—Chicken-pox is prevalent all over the world and is endemic in all large cities. There is no common *seasonal* incidence but a tendency to greater prevalence in autumn and winter.

Age.—It is essentially a disease of childhood. Although it is not common under the age of one year, congenital (intra-uterine) chicken-pox is known (Schuman, 1939), and cases have been described in the first month of life (von Reuss, 1920). Adults are affected not rarely. Thus 16·7 per cent. of 300 cases of chicken-pox examined as possible smallpox

were over eighteen years of age (Rolleston and Ronaldson, 1940). The disease is occasionally seen in middle-aged and elderly persons. The SEX incidence is equal. One attack usually confers *immunity* for life, but second attacks are known.

The CAUSAL AGENT is a filterable virus. By means of the electron microscope the virus particles have been shown to be rectangular, averaging 238 mμ × 210 mμ in size. The virus does not grow in developing eggs and has not been transmitted to small laboratory animals. Paschen (1919) and Amies (1933) demonstrated elementary bodies in the vesicle fluid. Van Rooyen and Illingworth (1944) showed that smears of the elementary bodies taken in the papular and early vesicular stages can be shown to be different from those of smallpox by their smaller size (0·125 to 0·175 μ) and difficulty in staining. Suspensions of these bodies are specifically agglutinated by the serum of chicken-pox convalescents. The portal of entry is the upper respiratory tract. INFECTION is mainly conveyed by air currents, but there is evidence that it can be transmitted by a third person or by infected articles.

INFECTIVITY is exceedingly high in the earliest stages of the disease, from at least twenty-four hours before the rash appears until the end of the first week. In the second week infectivity is slight, and it is probably absent after the tenth day (Gordon and Meader, 1929), although the dried crusts are still considered potentially infective. Infectivity towards the end of the incubation period has often been observed (Pickles, 1939). In one case infection was believed to have occurred *four days* before the rash appeared (Evans, 1940).

Symptomatology.—The incubation period is usually sixteen or seventeen days but may vary from thirteen to twenty days. Apparent shorter or longer incubation periods should give rise to suspicion of a missed case. In the vast majority of cases the eruption is the first sign. Occasionally febrile prodromal symptoms precede the appearance of the rash by twenty-four hours, especially in adults, but the patient does not feel better when the rash comes out, as in smallpox. A scarlatiniform *prodromal rash*, clinically identical with that of scarlet fever, is quite common in chicken-pox. Even more commonly a scarlatiniform rash *accompanies* the true rash. This may be a sensitivity rash or it may be due to streptococcal infection of a vesicle either in the mouth or in the skin. The *true eruption* probably commences first as an *enanthem* on the buccal and pharyngeal mucosa, although vesicles in this situation may be visible only when the eruption is profuse. On the mucous membranes, vesicles rapidly rupture, leaving small greyish white ulcers surrounded by an areola. The *exanthem* appears first on the trunk, generally the back, as macules which rapidly develop into papules and then into vesicles. The chest and abdomen are next invaded and then the face, scalp and limbs. The eruption comes out in *crops*, so that after two days all stages of the eruption may be seen on one site at the same time—macules, papules, vesicles, pustules and crusts. The order of appearance is also the order of density. Density is usually greatest on the back, abdomen and proximal ends of the limbs. The

distribution of the rash is *centripetal*, in contradistinction to that of smallpox which is *centrifugal*. There are more lesions on the trunk than on the limbs, and more lesions on the upper arms and thighs than upon the forearms and legs. Lesions may appear on the dorsum of hand and foot and even on the palms and soles, as in smallpox, but they are scanty compared with those in proximal and central situations. The lesions also appear unselectively on *concavities* and protected parts, such as the axilla and orbit rather than on exposed situations like the forehead and wrists (cf. smallpox). Like most rashes it clusters on areas of inflammation or irritation, *e.g.* sunburn. The number of pocks may be so few as three or four or amount to several hundred. There may be one to five successive crops. In profuse rashes the mucous membranes are usually involved, especially the mouth and pharynx, conjunctiva, vulva and prepuce.

The *elements* of the eruption are at first small pink macules which, in a few hours, become larger and darker maculo-papules and a few hours later become vesicles. The vesicles have certain characteristics: (1) they are superficial, being situated "on" rather than "in" the skin; (2) there may or may not be an areola—in the latter case the vesicles look like drops of water on the skin (glasspox); (3) many of the pocks are *oval* with long axis parallel to the natural folds of the skin; (4) they are unilocular. Later their contents become opalescent (pustules) and infection from skin organisms at this stage frequently causes an areola. Desiccation begins in the centre of the pustule as a small dry brownish spot. About the end of the fourth day a pock has become a dry scab or crust which after a variable time separates leaving a shallow oval scar at first pink in colour and later dead-white. Only a few of the deeper more infected pocks leave easily perceptible permanent scars. These scars, if of typical shape and distribution, form permanent evidence of a previous attack of chicken-pox. The degree of *constitutional disturbance* is in most cases slight or even trivial. Apart from the rare secondarily infected types mentioned below, it depends upon the extent of the eruption. In children, pyrexia is often absent, or slight, and the same applies to adults with scanty eruptions. Adults and some children, however, not infrequently have profuse eruptions with high temperatures and considerable malaise—a type of case often confused with smallpox.

Blood picture.—Holbrook (1941) has shown by serial blood counts that there is leucopenia with relative lymphocytosis from the end of the incubation period until the second or third day of the rash. This is followed by an absolute lymphocytosis during the eruptive stage. Lymphoblasts and prolymphocytes are commonly present indicating a stimulus to lymphocytic activity. Plasma cells may be present up to 6 to 8 per cent. The blood picture, however, should not be relied upon as a diagnostic feature.

Varieties.—Certain variations in development of the lesions occur. Sometimes they remain as papules for thirty-six hours or more, making early diagnosis more difficult. Some abort without becoming vesicles. In profuse eruptions vesicles may become confluent and enlarged to half

an inch in diameter. Occasionally a number of bullous or even pemphigoid lesions appear among the pocks, usually, by secondary infection with *staphylococcus aureus*. This form is known as *varicella bullosa*. Rarely a severe toxic form of chicken-pox occurs with hæmorrhages not only into the vesicles but also between the pocks and in mucous membranes, (*varicella hæmorrhagica*). *Varicella gangrenosa* is rare and highly dangerous. It occurs in (*a*) a *fulminating* and (*b*) a *subacute* form (Banks and McCartney, 1937). The fulminating form in two cases seen by the writer, one in the pre- and one in the post-sulphonamide era, was due to infection with hæmolytic streptococcus from the tonsils (type 23 in one case). In a fulminating case, not rapidly and adequately treated by chemotherapy, an area of purplish solid œdema and necrosis spreads rapidly from the infected vesicle to cover several square inches of surface. There is a serous exudation from the area but no pus, and an associated overwhelming septicæmia and toxæmia. The patient is prostrated from the outset, and may die in thirty-six to forty-eight hours. On the other hand, in a fulminating case treated early and adequately with sulphathiazole or penicillin the lesion soon ceases to extend, turns black and ultimately sloughs off a considerable area of cutis, the septicæmia and toxæmia meanwhile rapidly subsiding. The subacute type may be due to secondary diphtheritic infection which spreads sometimes from the anterior nares (Joe, 1928; Zahorsky, 1930). It is, indeed, a form of cutaneous diphtheria (*q.v.*), in which there are usually one or more slowly expanding ulcers covered by dry greyish black sloughs arising from the infected pocks. Accompanying toxæmia is slight, but after some weeks signs of post-diphtheritic myocarditis and paresis may occur. Such cases should be promptly investigated bacteriologically and treated with antitoxin.

Complications.—The most common in children are those due to secondary infection, *e.g. impetigo contagiosa* affecting the scalp or other region, and *impetigo bullosa* which may be confused with varicella bullosa. (In the latter, the bullous lesion evolves differently, drying in the centre like the other pocks.) Boils, abscesses or erysipelas may similarly develop. *Accidental or concurrent rashes* of scarlatiniform, morbilliform or urticarial type may occur as toxic or allergic phenomena secondary to the above forms of dermatitis. Infected pocks on the conjunctiva or in the neighbourhood of the eye were sometimes fatal in the pre-sulphonamide era from cellulitis, septicæmia and cavernous sinus thrombosis. Other very rare complications which have been recorded are laryngeal obstruction from pocks on the larynx, keratitis, nephritis, arthritis, purpura fulminans and interstitial (" atypical ") pneumonia with encephalitis and nephrosis (Waring, 1942). Otitis media is due to secondary streptococcal upper respiratory infection.

Nervous complications.—Underwood (1935) after an exhaustive study of 120 cases in the literature showed that apart from nervous prodromata including convulsions, the neurological complications chiefly consist of: (1) *meningo-encephalitis*, with early and dominant meningeal signs and a sterile spinal fluid which may or may not show pleocytosis;

(2) *encephalitis*, comprising 50 per cent. of the reported cases. It is by far the most important (cerebellar forms comprising ataxia, vomiting, speech changes, nystagmus, vertigo and tremor are most typical of varicella encephalitis and tend to differentiate it from other forms of post-infective encephalitis); (3) myelitis; (4) neuritis and polyneuritis. The onset in most cases is between the fourth and tenth day after the appearance of the rash. There is no definite pathological picture of perivascular demyelinization as in the case of post-infective encephalitis generally, although this type may occur. The prognosis is good (Dagnelie *et al.*, 1932). The mortality from encephalitis may be as low as 6 to 10 per cent., and sequelæ about 15 per cent. (Waring). Nervous complications in chicken-pox are very rare.

Varicella and herpes zoster.—Von Bokay (1894 and 1909) was the first to record a case of chicken-pox arising in a contact of herpes zoster after the correct incubation period. Many outbreaks of chicken-pox so caused have since been observed. A case of herpes zoster occurring in a children's ward should always be isolated. The opposite effect—herpes zoster occurring in a contact of chicken-pox—is also well known but is much rarer. The concurrence of herpes zoster and chicken-pox is not altogether rare. The writer has seen at least a dozen cases, three of them in 1943. In these cases a sparse eruption of chicken-pox occurred about a week after the onset of herpes zoster (usually ophthalmicus) in middle-aged and elderly subjects. It is now held that many if not all cases of herpes zoster are caused by the varicella virus invading the posterior root ganglia. This would be another example of neurotropism of the varicella virus. Certain bacteriological evidence also favours this view. Thus, Amies (1934) has demonstrated elementary bodies in the vesicles of herpes zoster which are apparently identical with those present in chicken-pox vesicles, and Netter and Urbain (1924) have demonstrated by cross complement fixation that identical antibodies are contained in the sera of patients with these diseases. A considerable degree of cross immunity has also been demonstrated by inoculation experiments with varicella and zoster fluid respectively (Lipochutz and Kundraditz, 1925). The above view, of course, relates only to varicellous forms of herpes zoster. It is not concerned with possible non-varicellous forms due to lesions of the nervous system other than viral.

Diagnosis.—An initial punctate erythema may lead to an erroneous diagnosis of scarlet fever. All punctate erythematous rashes, especially when there is no accompanying tonsillitis with exudate, should be carefully examined for the presence of a few discrete papules or vesicles on the trunk.

Diagnosis of a fully developed case of chicken-pox is easy; the difficulty is in the earliest stage. The following criteria are cardinal: (1) prodromal illness lacking or trifling; (2) centripetal distribution of the rash; (3) presence of the rash in concavities; (4) superficial elements including ovoid vesicles; (5) *cropping* of lesions with all stages present in one part at one time; (6) absence of chicken-pox scars. These criteria associated with the vaccinial condition, the absence of contact with small-

pox and of the special criteria for smallpox diagnosis (*q.v.*) should enable the differentiation between chicken-pox and smallpox to be made in most cases with confidence. Difficulties may, however, occur in much modified smallpox when only a few lesions are present. The smear test for elementary bodies may help in the differentiation between chicken-pox and smallpox (p. 1763).

The above criteria combined with the appropriate special features of each disease should also serve to differentiate chicken-pox from *papular urticaria* even when vesicles are found in the centre of some of the papules in this condition, from *erythema multiforme* of the bullous type, from *bullous impetigo*, and streptococcal *pemphigus* and from conditions associated with minute vesicles such as *scabies*, prurigo, cheiropompholyx and miliaria.

Treatment.—Most cases require no treatment beyond confinement in bed until the lesions have desiccated. Measures may be required to prevent secondary infection in children, *e.g.* covering the hands with gloves made of lint and splinting of the arms with cardboard to prevent scratching. Itching of the lesions, especially those on mucous membranes, *e.g.* the vulva, may be intense. It may be relieved by warm alkaline baths or by soothing and analgesic powders, or lotions such as calamine. The hair of the scalp should be cut short in boys and shampooed frequently. Lesions which become septic may be rapidly cured with antibiotic creams ; small septic lesions may be painted with $\frac{1}{2}$ per cent. gentian violet solution. The hair of the scalp should be shaved for a considerable area around the septic lesions. Dangerous infection with staphylococcus aureus, as in varicella bullosa, or with hæmolytic streptococcus as in cellulitis or fulminating varicella gangrenosa requires immediate sulphonamide and penicillin treatment in doses as for severe infections. Detachment of the scabs is facilitated by brushing lightly with carbolized oil.

Prophylaxis.—There is no reliable method of *specific prophylaxis*. Inoculation with varicella or herpetic vesicle fluid is not without danger, gives inconsistant results, and is not recommended. Convalescent serum has been proved to possess specific antibody but it has little or no value in practice. The isolation period need not be longer than fourteen days, and even less if the primary scabs have separated within that time. *Isolation*, concurrent disinfection of fomites and aseptic nursing technique must be particularly strict during the first week of the disease (p. 1745).

Quarantine of contacts is usually now disregarded in practice. Child contacts should be kept under observation for twenty-one days. In hospital they should be isolated if possible from other children from the tenth to the twenty-first day.

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VACCINIA

Synonyms. –*Fr.* Vaccination, *Ger.* Schutzpockenimpfung, *Ital.* Vaccinazione, *Sp.* Vacunacion.

Introduction.—Inoculation of smallpox from mild cases in order to confer immunity against severe forms of the disease was an ancient practice in India and China. One of these methods, variolization, was introduced into England in 1721. As practised in England, it consisted of scratching lymph into the arm from a vesicle in a previously inoculated person, never from an actual case of smallpox. Often a mild attack ensued which protected against the natural disease, and the practice became popular in the eighteenth century. But attacks were sometimes severe and even fatal and the variolized person was infectious to others. The practice fell into disuse after vaccination was introduced and it became illegal in 1840.

Vaccination was introduced by Edward Jenner in 1796. It had long been a common belief in Gloucestershire that milkers who contracted blistered sores on their hands through milking certain cows with ulcerated teats were rendered immune to smallpox. Jenner put these observations to an experimental test by inoculating a boy successfully with cowpox and subsequently finding him immune to inoculations of smallpox. Jenner's conclusion that cowpox or vaccinia protected against smallpox has been abundantly vindicated but his belief that the immunity endured for life has not proved correct. Re-vaccination at intervals of one to five years, according to the degree of exposure, is necessary to maintain immunity.

Relationship of vaccination and smallpox.—The virus of cowpox and that of smallpox are now believed to be identical, the former representing a strain or strains attenuated by passage through cattle. True variola can be transmitted to cattle and after several passages becomes so attenuated that upon re-inoculation into man a simple vaccinia

is produced (Haccins, 1908). Additional evidence of identity is obtained by inoculating either smallpox or vaccinia matter into the cornea of a rabbit, when a histologically identical type of keratitis is produced. Smallpox prophylaxis (vaccinia) therefore represents in principle active immunization with attenuated virus, this virus being a strain obtained after passage in animals. Vaccinia differs from smallpox in two important particulars: (1) it is not infectious (although contagious), and (2) it never reproduces smallpox. Vaccinia, though local in its eruption, is, nevertheless, a general disease. At the height of the eruption the virus can be demonstrated in the blood, naso-pharynx, spleen, and many organs including the brain. There are several strains of vaccinia virus, differing in potency. The ordinary dermal strain, if injected intra-cerebrally in rabbits, produces an encephalitis and by repeated passage in this way its neurotropism is increased (Levaditi and Nicholau, 1923). The strain thus produced is called neuro-vaccine and it is capable of producing gross hæmorrhagic and necrotic lesions in the human skin and organs, but not any increase in post-vaccinial encephalitis as known in man. Owing to its toxicity, however, its use has been abandoned. It is generally considered necessary to use a dermal strain for the preparation of vaccine material by which the risk of producing dangerous or generalized lesions is reduced to a minimum (Buddingh, 1937).

Preparation of vaccinia virus.—(1) *Vaccine lymph* is prepared by inoculating parallel linear scratches upon the shaved abdomen of calves or sheep with virus obtained from lesions produced in the rabbit. On the fifth day, the pulp from the vesicles is curetted off, mixed with 60 per cent. glycerine and stored in the cold for six weeks or more. This effects a great reduction in the number of bacteria present. Storage must not be too prolonged or the virus will become too attenuated and failures of vaccination occasionally occur. Thus glycerinated calf lymph as issued for use is *not a sterile product*; in addition to the virus it contains some skin organisms.

(2) *Elementary body suspensions* have been prepared from sheep lymph pulp by precipitation followed by filtration (Henderson and McClean, 1939).

(3) *Chick-embryo virus* is now obtained free from extraneous organisms by growing the virus on the chorio-allantoic membrane of twelve-day chick embryos (Woodruff and Goodpasture, 1931). This has the great advantage of a sterile product and may ultimately supersede calf-lymph. A disadvantage at present with certain strains is that the virus tends to become less virulent with continuous egg passage (Stevenson and Butler, 1933). This culture-virus may also produce sensitivity reactions in egg-sensitive individuals.

Technique of vaccination.—Age. Primary vaccination is best performed in infancy from two to six months of age. The risk of post-vaccinial encephalitis is then much reduced as compared with that in primary vaccination of older children or adults.

Number of insertions.—Before 1929, Public Vaccinators were directed to make four insertions of lymph, the aim being to produce an

area of scarring of at least half a square inch. In consequence of an increase of post-vaccinial encephalitis about that time and of the prevalence of *variola minor* in Britain, the Vaccination Order of 1929 recommended a single linear insertion with the minimum of trauma; scarification and cross-hatching were not advised. The duration of immunity following a single insertion is not yet established, but recent experience with importations of *variola major* suggests that it is considerably less than that following four insertions. After a single insertion immunity should not be presumed for more than one or two years. A single insertion is still the routine practice in Britain in the absence of epidemic smallpox. Should there, however, be no "take" at least two further attempts should be made at weekly intervals using three insertions on each occasion. When there is high probability of exposure to variola major, as in India, two or three insertions are probably more protective than one and vaccination should be repeated every one to two years. LYMPH. Probably the greatest cause of failure of vaccination in practice is the use of stale lymph. If stored at temperatures below 10° C. its potency is retained for fourteen days, but if stored at above 10° C. its potency after seven days cannot be relied on. It must be used immediately after receipt or stored in a refrigerator. SITE. The usual site is over the insertion of the deltoid. Goldberger (1920) and others recommended the inner posterior aspect of the upper arm as being less subject to friction and visible scarring; the disadvantage is the more severe axillary adenitis that may be produced. The thigh is often used in girls but this site is particularly subject to secondary infection and post-vaccination tetanus and it cannot be recommended (Armstrong, 1928). PREPARATION OF SKIN. Wash with soap and water followed by spirit or ether and allow to dry thoroughly before putting on the lymph. No antiseptic must be used on the skin.

METHODS. *Linear scratch.*—The capillary tube with ends broken off is placed in a rubber lymph ejector, and a drop squeezed out on to the cleansed skin. For two insertions, the drops should be $\frac{3}{4}$ inch apart. By means of a sterile round pointed sewing needle or a scarifier a superficial scratch is made $\frac{1}{8}$ to $\frac{1}{4}$ inch long through the drop of lymph without drawing blood. The scratch must penetrate through the epidermis. After a few minutes during which the lymph is soaking in, a narrow wheal should be visible on the scratch line. When this is seen the clothing may be replaced; if it is not seen, the scratch may be deepened or a new one made. No dressing is usually required. Dressings tend to retain moisture and favour the growth of skin organisms. The developing pock should be kept dry. It may be painted twice daily with mercuric chloride in spirit 1 in 1,000, or dusted with antiseptic powder.

Multiple pressure.—With a straight, bayonet-shaped needle held almost parallel to the skin, ten to thirty punctures are made through the drop of lymph and the whole thickness of the epidermis without drawing blood. The puncture must be effected by repeated pressures of the length of the needle against the stretched skin. The area of the punctures should not exceed $\frac{1}{8}$ inch in diameter. This method is much used in U.S.A. and is now officially recommended in Great Britain (Min. of Health, 1948).

Intra-dermal and subcutaneous injection. Sterile virus suspensions have been injected in this way in order to avoid vesiculation and scarring. Several observers (Henderson and McClean, 1939; Donelly, 1939) have shown that immunity is not produced unless vesiculation occurs. It is therefore not recommended.

Symptomatology.—In the *ordinary reaction* of primary vaccination, a papule appears on the fourth day, a clear vesicle with surrounding areola on the fifth day and umbilication of the vesicle on the sixth day. By the eighth day the vesicle contents are turbid, and by the tenth to twelfth day fully matured and purulent with an area of itching infiltration and axillary adenitis. From the eleventh to fourteenth day the pustule dries and begins to form a crust which separates in the third week leaving ultimately a depressed foveated scar. Constitutional symptoms increase with the age of the patient, the number of insertions and the amount of secondary infection. Splenomegaly is common. In the *accelerated reaction of re-vaccination* ("vaccinoid") speeding up and modification of the lesion occurs according to the degree of residual immunity from former vaccination. Thus the vesicle may appear about the third day and dry up without pustulation. In the *immediate reaction*, the speeding up process is carried further. A small itching papule appears about the third day and rapidly aborts without vesiculation. This transitory erythema, though often shown by immune subjects, may not necessarily indicate immunity. It may be a sensitivity reaction to calf lymph since it can frequently be produced by inactivated lymph. It should not therefore be described as the "reaction of immunity" (Marsden, 1944).

Complications.—Those due to vaccinia itself.

(*a*) *Generalized vaccinia.*—This is very rare. The incidence is about 1 in 100,000 vaccinations and the mortality 1·2 per million vaccinations. It occurs almost solely in primarily vaccinated children. It is due to an abnormally low degree of natural immunity to the vaccinia virus. It appears most commonly from the ninth to fourteenth day, as a crop of papules which mature into vesicles, pustules and crusts and are scattered so widely as to exclude auto-inoculation from the vaccination site. The distribution is haphazard and does not conform with that of smallpox (Jubb, 1943).

(*b*) *Auto-inoculation* of vaccinial matter from the original vaccine lesion, causing secondary pocks on such sites as the nose, ear and lips.

(*c*) *Post-vaccinial eruptions* are relatively common and are due in most cases to absorption of toxins or allergens from the vaccination site. They may take the form of papular urticaria, erythema multiforme, or scarlatiniform rashes (Bloch, 1942).

(*d*) *Eczema vaccinatum* occurs in vaccinated persons with a history of eczema or in children suffering from eczema who are in familial contact with a vaccinated person. On the eczematous site, vaccinia-like vesicles appear and later may spread to healthy skin and other organs. This is one form of the condition known to dermatologists as "Kaposi's varicelliform eruption," the other form being *eczema herpeticum* in which the eczematous

area is infected with the virus of *herpes simplex*. *Eczema in the eruptive stage is one of the chief contra-indications of vaccination.*

(*e*) *Encephalitis.*—This serious but rare complication of *primary* vaccination is similar clinically and histologically to that which occurs after smallpox and measles. It develops six to fourteen days after vaccination; its symptomatology is as described for post-measles encephalitis (p. 1728); Babinski's sign is commonly present, and the spinal fluid shows an increase of mononuclear cells; its mortality is high, 25 to 30 per cent. In Conybeare's series (1948) the following four clinical groups were recognized: (1) myelitis without encephalitis 10 per cent., (2) encephalomyelitis 10 per cent., (3) encephalitis 75 per cent., and (4) meningeal reaction 5 per cent. Its pathogenesis is unknown, but appears to be independent of the action of any particular lymph. Its incidence varies in different countries and at different times in the same country. In recent years its incidence in England and Wales has been between 1 in 50,000 and 1 in 100,000 vaccinations. In Glasgow out of 500,000 vacinations performed within a fortnight in 1942, there were seven recognized cases of encephalitis (Anderson and McKenzie, 1942). In Fife, in the same year, however, out of a group of 52,772 vaccinations eight cases occurred (Fyfe and Fleming, 1943). In Holland the incidence for a few years at one time was as high as 1 to 4,028 vaccinations. No cases have been recorded in infants under one month, extremely few under three months and but a few more under six months of age (Travis, 1938). Treatment by intravenous or intramuscular human serum from a person recently vaccinated was believed to have had some success (Horder, 1929; Hekman, 1930), but its value has not been established.

In view of these facts, vaccination during early infancy should be the aim. Primary vaccination of school children should be avoided as far as possible, except where contact with smallpox is a possibility, when the risk must be taken. Insertions in such cases should, however, be limited to one or at most two.

Complications accidentally acquired.—These are mainly the result of secondary infection, *e.g.* erysipelas, boils, bullous impetigo, etc. Tetanus is very rare. It appears about twenty days after vaccination and is probably associated with contamination from non-sterile dressings and shields (Anderson, 1915). These complications can usually be avoided by proper after-care of the vaccinated arm and by restriction of physical effort during the active stages of the reaction.

Indications and contra-indications.—Smallpox can be so serious a disease that every healthy infant at the age of two to six months should, as far as possible, be protected from it by vaccination. Although absolute protection cannot be guaranteed for more than two years, it is reasonably safe practice for re-vaccination to be performed at the age of entry to school and again at any subsequent time when the risk of exposure to smallpox is incurred. This programme entails little risk of encephalitis, and if applied universally would render negligible the problem of smallpox. If vaccination is not performed in infancy, the slight risk associated with primary vaccination has often to be faced

later, on entry to any public service, *e.g.* medical, nursing, civil and defence forces, and, of course, on any exposure to variola major. Since vaccinia is a general disease, however, it should, without hesitation, be postponed when a child is not in good health. Eczema, syphilis, and active tuberculosis are perhaps the chief contra-indications, but any septic condition of the skin and any febrile attack or recent exposure to acute fevers justifies postponement.

Immunity to smallpox should never be presumed if vaccination does not " take." If the lymph is active and is properly absorbed, even persons with high-grade immunity usually develop a small itchy papule. The most frequent causes of failure of vaccination are inactive lymph and errors of technique. In case of failure, vaccination should be repeated again and again with fresh lymph.

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SMALLPOX

Synonyms.—Variola. *Fr.* Variole, petite verole, *Ger.* Pocken, Blättern, *Ital.* Vajuola, variola, *Spa.* Viruela, *Dutch.* Pokken.

Epidemiology.—Smallpox is an infectious disease in which the widest variations in clinical severity and infectivity are met with in practice. These variations depend both upon differences in the virus itself and upon the degree of immunity of the subjects attacked. Two strains of the virus stand out pre-eminently, because in non-immune subjects they regularly produce distinctive clinical syndromes which have been well-named *variola major* and *variola minor.* The former is the " classical " or " Asiatic " type, the cause of many devastating outbreaks of highly infective and highly fatal disease, with its main reservoir of

infection in India, China and Russia. Variola minor has also produced widespread disease in many countries, but of a benign nature, with little tendency to malignancy in the prodromal phase or to pustulation in the eruptive phase, and with lower grade infectivity. It is sometimes called the " American " type, and its chief foci of infection are U.S.A., Canada, Brazil, the West Indies and South Africa. It prevailed in Britain during the years 1922 to 1934, causing many thousands of cases, and spreading slowly from one area to another. Its synonyms include alastrim (Brazil), amaas, Kaffir-milkpox (South Africa), white-pox and para-smallpox. Although these two variants of smallpox have been shown in many outbreaks to breed true, they not infrequently exist side by side. It is then not always possible to distinguish them clinically since *v. major* is so often modified by vaccination, and *v. minor* can, in rare cases, produce a confluent form of the disease. In the majority of non-immunes, however, the two varieties can be distinguished both clinically and epidemiologically. Vaccination protects against both, but for a longer period and to a higher degree against *v. minor* than against *v. major*. It was observed, for example, in the Leicester outbreak of some 3,000 cases of *v. minor* in 1931–2 that only two cases occurred amongst men who were vaccinated during the war of 1914-18. Vaccination, therefore, gave almost complete protection for at least thirteen years, in spite of a degree of exposure which was often intimate, since the wives of many of these ex-service men contracted the disease. The period of effective protection against *v. major* is usually much shorter (p. 1752).

Age.—No age is exempt, from the infant *in utero* to the old. In practice, the ages of those attacked are chiefly affected by the vaccinial state of the population. Before the vaccination era, the disease was chiefly one of infants and young children. When infant vaccination was widely carried out in this country in the latter half of the nineteenth century, young persons and adults were more affected than children. In the present century, as a consequence of the neglect of infant vaccination, the incidence among children has again been high.

Congenital smallpox.—A child may be born scarred from having the disease *in utero*, or with the disease in full bloom or in the incubation stage, the " symptoms " in the last case starting a few days after birth. Infection does not, however, invariably pass from a variolous mother to the fœtus. The child may be born free from the disease and later be successfully vaccinated. Sometimes maternal smallpox is well advanced before the fœtus becomes infected. In twin pregnancies one infant has been known to be infected and not the other. The prognosis in congenital smallpox is grave.

Season.—The disease occurs in all climates and seasons, but is most prevalent in winter in northern latitudes and in the dry season in tropical climates.

Transmission.—The chief portal of entry is the respiratory tract. The alimentary tract is an alternative route, and inoculation through the skin has also been demonstrated. Overcrowding and common upper respiratory infections tend to favour transmission. Infectiousness in the

incubation period has not been conclusively demonstrated (cf. chicken-pox). The prodromal stage is generally believed to be infectious, possibly from the enanthem in the mouth which may be present towards the close of this period. It is practically certain, however, that the most infective period is in the early stage of the true rash, and that infectivity depends chiefly upon the density of the rash. " The curve of infective power rises to its maximum at the onset of maturation and subsequently falls with a steep decline " (Cameron, 1932). The virus is contained in the dried crusts and withstands desiccation for at least two years. It can be transmitted by air currents containing droplets or dust, by infected third persons, or by infected articles (fomites). An outbreak in this country was traced to infected bales of cotton imported from Egypt. Smallpox corpses are highly contagious, as many undertakers have found. The theory of aerial convection of smallpox over distances up to one mile from smallpox hospitals was advanced by W. H. Power (1880–84). This theory has been vigorously disputed on the grounds that, in a few of these cases occurring within the zone of the " hospital influence," illicit contacts between the hospital staff and the affected persons were proved to have taken place. A final conclusion on this subject has not yet been reached, but it is certain that variola major, at least, possibly more than any other disease, tends to spread for considerable distances from a focus of infection, and especially from a hospital where cases are under treatment.

Bacteriology.—The causal organism is a filterable virus which has been identified with the elementary bodies of Paschen (1906). These are found alike in the vesicles of smallpox and vaccinia (Ledingham, 1931). Guarnieri's (1892) inclusion bodies within the cytoplasm and the intra-nuclear inclusion bodies are believed to be either aggregates of the virus or products of reaction of the cell to the virus (Rivers, 1927). Some of them do not contain the virus. A definite difference in the histopathology of intra-nuclear inclusion bodies in alastrim and smallpox respectively has been reported (Torres, 1925), but this may not signify more than a different reaction on the part of the cell to the two strains of virus. On the other hand, pure suspensions of elementary bodies from *v. major* and *v. minor* show cross-agglutination with the serum of patients suffering from *v. minor* and *v. major* respectively (Amies, 1932). Van Rooyen and Illingworth (1944) were able to recognize the elementary bodies of smallpox by their size (0·25 to 4·0 μ) and arrangement in smears made from papules and early vesicles in 80 cases of all grades of severity. The place of the smear test in differentiation between chicken-pox and smallpox has been further defined by Downie (1947).

Blood changes.—There is a slight leucopenia with relative mononuclear increase from the onset of the disease until about the second day of the eruption when polymorphonuclear leucocytosis appears and continues during the pustulation and crusting periods. The eosinophils in severe cases are increased during the desquamation stage in convalescence. According to Nicholau (1928) there is a reduction of the platelets and an increase in the coagulation time.

Symptomatology.—*The incubation period* in variola major is usually remarkably constant at twelve days, or to the outcrop of the true (focal) rash fourteen days, with a minimum of eleven and a maximum of seventeen days. Ricketts (1908) preferred to work with the fourteen-day period in investigating a case, because of the difficulty in mild cases of fixing the time of onset and also because of the variability in the length of the prodromal period. In inoculated smallpox the incubation period is shorter, seven to nine days. In variola minor on the other hand, the incubation period is sometimes longer than the above and was noted by the writer on several occasions during the Leicester outbreak of 1931–2 to be as long as twenty-one days. The clinical stages of smallpox are (1) the prodromal or toxæmic phase (primary fever) from the onset of symptoms to the appearance of the true rash and (2) the eruptive stage (secondary or septic fever) during which the true rash passes through its evolution from papules to vesicles, pustules and crusts. The clinical course of both varieties of smallpox may be profoundly modified by vaccination. In unvaccinated subjects the course of *v. major* is usually quite different from that of *v. minor*, and the following description is of typical unmodified *v. major*.

Prodromal stage.—The attack begins suddenly with pain in the epigastrium, frequent vomiting, headache, high pyrexia and pains in the limbs. Backache, a prominent symptom in adults, is not common in children. Abdominal pain and vomiting may give rise to an erroneous diagnosis of appendicitis, for which laparotomy has been performed in several cases known to the writer. Profuse sweating is common. In severe cases, convulsions and delirium may occur, succeeded by drowsiness or coma. The tongue is thickly furred, the breath offensive, the bowels constipated, except in infants who usually have diarrhœa. The spleen may be palpable. This is the toxic phase of the disease, sometimes called the "primary fever." It is difficult to distinguish from influenza except that respiratory symptoms are less prominent. Some throat or bronchitic cough may appear towards the end of the prodromal period owing to the presence of the enanthem in fauces and bronchi. The period usually ends on the third or fourth day, when the temperature falls, either in a well-marked remission or even to normal for a day or two. At this stage patients feel so much better that they may actually try to get about, and they have even been known to attend a doctor's surgery. A severe prodromal stage, usually but by no means invariably, is followed by a severe eruptive stage; sometimes, indeed, the ensuing eruptive stage is quite mild. Prodromal rashes are uncommon in children. They are of two kinds: (*a*) *erythematous*, usually of scarlatiniform, morbilliform or urticarial type and distributed irregularly on the trunk, face and limbs; (*b*) *hæmorrhagic*, either petechial or purpuric, and usually located in the groins and flanks ("bathing drawers area") and also in the axillæ. The hæmorrhagic prodromal rash is characteristic of the most fatal form of hæmorrhagic or malignant smallpox.

Eruptive stage.—The focal rash appears, with rare exceptions, on the third or fourth day on mucous membranes and skin. On the latter,

the sites of first appearance are the forehead and wrists. The first elements are macules which, in a few hours, become hard shotty papules, deeply set in the skin, and surrounded by a narrow areola. The papules continue to appear on the face and scalp, arms, trunk and legs, *in that order*, until the whole body is covered. The papular stage usually lasts for about three days before vesiculation is seen, and during this period the disease has often been mistaken for measles. Vesiculation is usually complete by the sixth or seventh day. The vesicles are circular, multilocular, contain clear fluid and have a dome-shaped or flat top and umbilicated centre, surrounded by a red areola. Within forty-eight hours of their formation the contents, commencing at the periphery, become turbid, the vesicles enlarge to $\frac{1}{4}$ inch or more in diameter, the areola disappears, and by the tenth day the pustules are fully formed. This is the stage of *maturation*. Coincident with the formation of pus the rise of temperature known as "secondary or septic fever" takes place, the duration and extent of which depend upon the profuseness of the rash, the amount of pus formed in the skin and the time taken for the lesions to dry up into crusts. The latter process usually takes eight or nine days. Separation of the scabs continues from about the eighteenth to thirtieth day. Certain deep-seated crusts or "seeds," especially on palms and soles, may be long in separating. Circular scars are left, at first pigmented, and later white and foveated.

The order, noted above, in which the focal rash appears is of extreme importance in diagnosis. First the *enanthem* appears in the mouth, fauces, pharynx, larynx and bronchi, and may give rise to sore throat, hoarseness and cough. The mucous lesions develop and ulcerate rapidly and are generally more advanced than those in the skin. Lesions in the mouth are important in differential diagnosis, but not as between smallpox and chicken-pox. The enanthem *unfurls itself* in rapid but orderly progression throughout the body. There are only slight differences in the age of the lesions in any one part, but as much as twenty-four hours between the parts where the lesions appear early, *e.g.* the face and those where they appear late, *e.g.* the legs and feet. Thus, *on any one part of the body* the rash is practically *homogeneous*, that is, all papules, all vesicles, all pustules or all crusts. Nothing comparable to the "cropping" of chicken-pox, with its variety of lesions in one part at one time, is seen.

When fully developed, the focal rash is of *centrifugal* distribution, with more lesions on the limbs than on the trunk and more lesions in the distal part of the face and of the limbs than upon the proximal parts. Thus, forearms, hands and fingers are more densely covered than the upper arms, and similarly the legs and feet than the thighs. Again, on the back and upper chest, the lesions are more crowded than upon the abdomen. Another important point in distribution is that the rash seeks out those sites where there is exposure to air and the friction of clothing, and avoids hollows and protected parts. Thus, over convexities and prominences, lesions are denser than on the adjoining skin. Such prominences include the forehead, malar bones, nose, chin, the

sternomastoid, clavicle, back of the neck, scapula, prominent tendons and even lines of pressure from waist belts, braces or garters. In both these respects, centrifugal distribution and the density over prominences, smallpox is clearly distinguished from chicken-pox. Chicken-pox indeed is characterized by the exact opposite—a rash with centripetal distribution and one that does not avoid concavities like the axilla.

Unmodified smallpox generally conforms with the pattern described above, but there are considerable variations in severity both of the toxic phase and the septic phase. The chief varieties are the *hæmorrhagic*, the *confluent* and the *discrete*.

Hæmorrhagic smallpox is of two kinds. (*a*) The purpuric or malignant form (black smallpox) is invariably fatal from grave toxæmia before the seventh day. It is characterized by extreme prostration, a fluttering pulse, generalized loss of muscular tone, expressionless face, mental clearness, rapid respiration without pulmonary involvement, nauseating fœtor oris, profuse hæmorrhages from the skin and mucous membranes within a day or two of onset and failure of the focal rash to develop properly even up to the sixth day (Wilkinson, 1943). It has thus many features in common with the pure adrenal syndrome in fulminating meningococcal septicæmia, although adrenal hæmorrhage has not to the writer's knowledge been reported. (*b*) The pustular hæmorrhagic form, in which hæmorrhage of lesser degree appears in and below the pocks of the focal rash, is usually but not always serious (cf. post-measles staining, p. 1725).

Confluent smallpox also exhibits degrees of severity. The worst is the highly fatal but rare type in which the focal lesions are confluent on the face in the papular or vesicular stage. More common is the type in which confluence occurs by expansion in size of the lesions in the pustular stage. *Discrete* smallpox may be classified in diminishing grades of severity according to the number of pocks on the face: (*a*) more than 500, (*b*) between 500 and 100, (*c*) less than 100 (Ricketts, 1908).

Modified smallpox is of various kinds. The usual source of modification is the partial immunity resulting from old-standing vaccination or re-vaccination. Vaccination cannot be relied upon to protect from *v. major* for more than two years. Ricketts showed that the protection against smallpox waned in the three stages: (1) that against the toxic phase, (2) that against the number of lesions in the focal rash, and (3) that against fully developed muturation. Certain persons who are well but not fully protected by vaccination suffer from *variola sine eruptione* when brought into close contact with a highly virulent strain of variola major: that is, they suffer from the toxic phase only, their vaccinial protection against that phase having lapsed (Conybeare, 1939; Bowe, 1942). Stages (2) and (3) are generally concurrent, but the faculty of modifying the lesions is retained long after protection against numerical severity is lost. Thus, there is a stage in modification when the elements of the rash may be extremely numerous and yet may dry up rapidly without maturing and this is accompanied by little or no secondary

fever. Such a case would clinically resemble one of *variola minor*. These three degrees of modification are the result of differential residual protection from vaccination. *Variola minor*, however, is modified smallpox of a different kind—due to a fixed loss of virulence in a particular strain of the virus. It produces a mild disease even in the unvaccinated, sometimes so mild that the eruption is limited to one or two spots. The primary fever is generally milder than that of *v. major*, but it is by no means insignificant, and has been known to be accompanied by hæmorrhagic rashes and even to be fatal from toxæmia (Marsden, 1936). The chief difference from *v. major* is seen in the more rapid evolution of the focal rash. Pustulation is present on the fourth day and early crusting established on the sixth or seventh day of the eruption. This means that the lesions do not expand to their normal size, and that pus formation, septic intoxication, secondary fever and scarring are slight or absent. In addition to these features, the incubation period is often prolonged, complications are few and relatively trivial and mortality is practically nil. In other respects, such as the prodromal illness, the distribution and shotty circular character of the lesions, *v. minor* and *v. major* do not materially differ.

Complications.—The most common are septic *skin* conditions—boils, abscesses, carbuncles, bedsores, erysipelas and gangrene of various parts of the skin, with associated loss of hair and suppurative adenitis. These appear during the scabbing stage or soon after. *Eye* complications are seen chiefly in the form of styes, blepharitis and conjunctivitis. These may be so severe that the cornea becomes invaded with consequent corneal ulcers and opacities or even panophthalmitis and blindness. Iritis and choroiditis are rare. Subconjunctival and retinal hæmorrhage may occur in the hæmorrhagic form. *Ear* complications include pustular dermatitis of the pinna and otitis media. *Respiratory*—œdema of glottis, bronchitis, broncho-pneumonia and empyema may all be consequences of the pustules on the mucous membranes. *Myocardial degeneration* is always present in severe toxic cases. *Thrombophlebitis* may occur in convalescence as in any severe fever. *Osteomyelitis* has been described particularly in children, and it may be accompanied by arthritis particularly of the elbow-joint. *Phimosis* may occur in children as a result of cicatrization on the prepuce. *Albuminuria* is common in the early stages but nephritis is rare.

Encephalomyelitis in its symptoms, course and pathology is similar to that following vaccinia (Marsden and Hurst, 1932) and measles. It begins five to thirteen days after the appearance of the focal rash, with pyrexia, disturbance of speech, twitchings, convulsions, drowsiness or coma, and various paralyses may supervene. The mortality may be as high as 50 per cent.

Morbid anatomy.—The pocks are widespread in the skin and in the mucous membranes including the upper part of œsophagus, rectum, vagina. The liver and spleen are enlarged and cell degeneration and necrosis may be found in the testis. In the hæmorrhagic form, mucous and serous hæmorrhages are widespread, together with ecchymosis around

the kidneys, and into the joints and uterus. Adrenal hæmorrhage does not appear to have been reported.

Diagnosis.—The *prodromal* stage, except in the hæmorrhagic form, cannot be certainly distinguished from influenza or other continued fever. Backache is an unreliable symptom in children. Abdominal pain may be prominent in children and has led to an erroneous diagnosis of appendicitis. Prodromal rashes are rare in children. A history, together with scars, of recent vaccination would be strong evidence against smallpox. In the *eruptive* stage, confusion is apt to arise with chicken-pox, measles, typhus fever and certain skin diseases. The procedure in making the examination is to look for vaccination marks, inspect the mucous membrane of the mouth and fauces, survey the whole area of the skin, to note the distribution of the eruption, whether centrifugal, centripetal or other and whether present in areas exposed to friction or in hollows, and lastly to examine carefully the character of the individual lesions. The differentiation from *chicken-pox* has been discussed in the section on chicken-pox.

The greatest difficulty occurs with the sparse eruptions of much modified smallpox. Two main points should be settled: (1) Is the rash more profuse on the extremities? (2) Did the temperature drop and the patient feel much better when the rash appeared? If the answers are both in the affirmative smallpox is likely. It may be confirmed by (*a*) centrifugal distribution, with relative freedom of the abdomen from lesions; (*b*) lesions in the same stage in any one place; (*c*) circular, deep-set, shotty papules or vesicles (test in an area where the skin is soft); (*d*) the rate of maturation of the rash—thus papules may last three days but not longer; pustulation never occurs as early as the third day. In *measles*, the Koplik's spots on the buccal mucosa near the molar teeth are diagnostic. It is the confluent case of smallpox in the papular stage with profuse rash on the face, suffused eyes and cough that is apt to be confused with measles. Measles of corresponding severity would always show Koplik's spots, usually very numerous. Typhus fever in children is often mild and difficult of diagnosis. The rash, however, does not come out until the fifth day, appears first on the trunk and rarely affects the face at all. In *papular urticaria* lesions are few or sparse on the face, are never in the mouth, and have a tendency to aggregate around the ankles; some of them may have minute conical vesicles at the summit of the papules; wheals and scratch marks are common. *Erythema multiforme*, of bullous type affects mainly the limbs and trunk, rarely the face; the lesions tend to be much larger in size and more superficial in character than those of smallpox. The papulo-pustular iodide and bromide *drug rashes* and the papular or erythematous sulphonamide rashes do not conform with the smallpox characters and distribution. Acute eczema, vesicular and pustular dermatitis, impetigo, scabies and dermatitis herpetiformis have all been mis-diagnosed as smallpox. In all these cases, a careful history is of first importance.

Laboratory diagnostic tests.—These are not required as a routine since the diagnosis can confidently be made on clinical grounds, in all

but a small proportion of cases. They also require the specialized technique of a virus reference laboratory. In the *papular and early vesicular stage* two methods are available: (1) microscopic examination of smears for elementary bodies, and (2) the culture of virus (from smears) in the chorio-allantoic membrane of developing eggs. In the *vesicular* and *pustular* stages, besides the above two methods, a third is available—complement fixation between the fluid from the pocks, as antigen, and the serum of a rabbit immunized against vaccinia, as antibody (Craigie and Tulloch, 1931). When the laboratory has this high titre antiserum in stock the result of this test can be known within twenty-four hours. Thus it may be of value for early and retrospective diagnosis. In the *crusting* stage two tests are available: (1) complement fixation and (2) test for antibody in the blood serum of the patient. After the crusting stage, only the test for antibody in the blood serum is valid and it is not applicable to persons who have been vaccinated.

Prognosis.—There are three chief factors governing the prognosis: (1) the vaccinial condition; (2) the nature of the attack and certain of the symptoms; and (3) the character of the epidemic.

(1) This is the most important factor. During the years 1901–3 unvaccinated children under fifteen years of age admitted to the London smallpox hospitals numbered 1,719, with 533 deaths, a case fatality rate of 31 per cent. Over the same period, 479 vaccinated children were admitted, with six deaths, a case fatality rate of 1·2 per cent. In vaccinated children under ten years of age, there are few deaths from smallpox.

(2) Confluent or profuse eruptions have an unfavourable prognosis (pre-penicillin mortality 40 to 50 per cent.) except in those with sufficient residual vaccinial immunity to modify the maturation of the lesions (p. 1760). The mortality in discrete *variola major* has been 6 to 8 per cent. Purpuric or malignant smallpox is invariably fatal. Hæmorrhagic pustular smallpox has a prognosis depending more on confluence than on the hæmorrhage. Profuse mucous lesions on fauces, larynx and bronchi may lead to broncho-pneumonia—a grave complication. A severe initial stage is not necessarily followed by a severe eruptive stage. A mild initial stage is always of good prognosis.

(3) The virulence of the strain of the virus varies considerably in different epidemics, particularly of *v. major*. In *v. minor* the mortality is always very small. It was only 0·25 per cent. amongst 13,686 cases treated in a London hospital from 1928 to 1934 (Marsden, 1936).

Treatment.—When a case is suspected to be smallpox, the medical officer of health should at once be informed. If the diagnosis is confirmed, the patient will generally be removed to a special smallpox hospital, and all contacts should be vaccinated on the same day. The house and its contents, including all clothing likely to have come into contact with the patient, should be thoroughly disinfected.

In the smallpox hospital, the patient is surrounded by a barrier of immunized persons, all members of the staff and all entrants to the hospital having been vaccinated or re-vaccinated. This, in itself, forms

a considerable measure of protection to the community. Nevertheless, smallpox is so infective that secondary cases are apt to arise in the neighbourhood of the hospital (p. 1757). Accordingly, the staff is permitted only occasional leave from the hospital, and must stringently disinfect themselves before going out.

Skilled nursing for the patient is very important, especially the toilet of the mouth, care of the skin, prevention of bed-sores, adequate fluids and nourishing diet. A sorbo rubber mattress or water bed is desirable and a bed with cot sides as a means of restraint for a delirious patient. Sedatives, *e.g.* chloral, barbiturates, paraldehyde and hyoscine are usually required in *v. major* as well as analgesics and hypnotics, *e.g.* somnifaine, pethidine or morphine. For the skin lesions, painting with a solution of potassium permanganate of moderate strength in the papular and vesicular stages is virucidal. Penicillin or other antibiotics should be given from the vesicular stage onwards in order to reduce pustulation, modify the secondary fever and prevent septic complications. If there is much irritation of the skin, alkaline or calamine lotion compresses or a soothing dusting powder may be useful. In profuse eruptions with much œdema surrounding the lesions, the writer has found continuous hot baths for an hour or more at a time to be most soothing to the patient. Deodorants are often necessary in a smallpox ward on account of the foul stench. Xylol in doses of 60 to 120 minims daily, strongly recommended by Teissier (1922), is a toxic drug now superseded by penicillin and other antibiotics. Convalescent serum and Finsen's red light treatment have not fulfilled expectations and are not recommended.

The *isolation period* for patients should extend until all crusts have separated and all cicatrices, ulcers or abscesses have healed.

Quarantine.—Contacts will be kept under supervision for sixteen days from the last exposure to infection, but it is not generally necessary to curtail their liberty.

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RUBELLA

Synonyms.—German measles. *Fr.* Rubéole, *Ger.* Röteln, *Ital.* Rubeola, *Dutch* Roode Hond.

Epidemiology.—Rubella is a specific mild infectious disease with a long incubation period and characterized by a pink macular rash, posterior cervical glandular enlargement and slight catarrhal and constitutional symptoms. It is quite distinct from measles and scarlet fever, although in certain cases confusion may arise in the differential diagnosis.

The causal agent is a filterable virus which can be obtained from pharyngeal washings when the eruption is at its height. The disease can be transmitted by spraying such filtered washings into the throats of susceptible persons. Infectivity is relatively slight and of short duration —probably not more than five days from onset. Transmission is by direct contact, probably droplet infection, and not, as far as is known, by fomites, third persons or carriers. The disease occurs in limited local epidemics, usually in spring and early summer. Its seasonal incidence does not correspond with that of measles or that of scarlet fever, but considerable over-lapping occurs. Occasionally, as in the spring of 1940 in England when crowded military camps and billets favoured transmission among susceptibles, extensive epidemics arise of a rather more severe character with fever of several days' duration, general glandular enlargement, tonsillitis, rheumatic sequelæ, encephalitis and occasional relapses (Bennett and Copeman, 1940). Such clinical severity is, however, rare in children. The disease is not uncommon in infancy but is most frequent between the ages of five and fifteen. Many children, however, escape the disease, and it is commonly contracted in adult life from the second to the fourth decade.

Symptomatology.—The incubation period is long, generally about seventeen days. The limits are probably fourteen to twenty-one days.

Prodromata.—Children seldom show symptoms before the appearance of the rash, although occasionally vomiting, slightly choked nose, sore throat or pain in the gums, with mild pyrexia precedes it by twenty-four hours or so. Enlargement of the posterior cervical, occipital and mastoid glands may also appear in the prodromal period.

Exanthem.—In the majority of cases, the rash is the first indication of the disease. It consists typically of small discrete pink macules, 1 to 2 mm. in diameter, appearing first on the face and quickly invading the trunk and, up to twenty-four hours later, the limbs. The colour is usually paler than the bright red rash of scarlet fever, or the brownish red rash of measles. The rash fades, usually within twenty-four to forty-eight hours, in the order of its appearance. Thus it may be quite visible for a time on the legs, after it has faded from face and trunk. In the severe type of case

noted above, the rash may be present for four or five days. It may coalesce into small blotches, but very rarely assumes the characteristic large crescentic blotchy appearance of the measles rash. A variation of considerable importance is the *scarlatiniform type* of rubella. This is probably due to confluence of the rash over large areas, often the whole of the trunk, giving a uniformly red or even a punctate scarlatiniform appearance to the eruption in those parts. This tends to occur on the second day of the rash. In these cases the rubella rash " resembles measles on the first day and scarlet fever on the second day." Desquamation of a powdery kind, especially on the face, occurs in severe cases with prolonged rash, but is not a common feature of rubella.

Enanthem.—There is no typical enanthem in rubella, but discrete red spots 1 to 2 mm. in diameter are occasionally seen on the palate (Forchheimer, 1898) and even on the buccal mucosa concurrently with the exanthem. Koplik's bluish white dots are never seen.

Lymphadenitis.—Enlargement and tenderness of the posterior cervical and sub-occipital glands are very characteristic. A row of glands about the size of peas and beans can usually be palpated along the posterior border of the sterno-mastoid muscle, and they are distinctly though slightly tender. General glandular enlargement may be present but is more typical of the severe case. The glandular enlargement often persists for a week or two, but tenderness disappears in a few days. The spleen is quite often just palpable in children.

Constitutional symptoms are generally slight, with little or no pyrexia. The child does not appear ill. The throat is dry and uncomfortable, faucial inflammation slight, nasal mucosa swollen but not discharging, and conjunctivitis definite but slight. At the end of two or three days all symptoms and signs have disappeared. Variations of this general clinical picture occur. A severe type with tonsillitis, aching of gums, considerable toxæmia and complications has been referred to as characteristic of some epidemics. On the other hand, many cases are even milder than that described, and as in most infectious diseases " formes frustes " occur. Thus " non-eruptive rubella " has been described, characterized by adenitis, conjunctivitis and coryza without a rash and occurring after intimate exposure to the infection and the correct incubation period.

Blood changes.—The blood picture is very similar to that of measles—leucopenia in the early eruptive stage followed by lymphocytosis, with plasma or Türk cells in even larger numbers than in measles. These cells are not constantly present in sporadic cases (MacBryde and Charles, 1935), and their absence does not negative a diagnosis of rubella. The blood picture is usually sufficient to distinguish between rubella and scarlet or glandular fevers, but not between rubella and measles.

Complications and sequelæ are rare and generally limited to the severer epidemics. Such rheumatic accompaniments as muscular and joint pains, serous arthritis and even carditis have been noted (Bennett and Copeman), but it is possible that these were manifestations of intercurrent acute rheumatism in such circumstances. Otitis media is the result of intercurrent hæmolytic streptococcal infection. Post-infective

encephalitis similar to that seen after measles, smallpox and vaccinia has been reported in at least sixteen cases, of which two were fatal. Most of the eleven cases reported by Merritt and Koskoff (1936) were in children aged five to fifteen years; the interval between the appearance of the rash and the onset of nervous symptoms was from two to six days; meningeal signs were present in six. In encephalitis, the spinal fluid contains some 10 to 150 lymphocytes per c.mm. and 60 to 180 mgm. protein per 100 c.cm.: chloride and sugar are near normal. The writer has encountered one typical case in which pyrexia, delirium and coma appeared four days after the rash. The coma, at first very deep, passed off in thirty-six hours and recovery rapidly ensued (Banks, 1941). The necropsy described by Taylor (1937) revealed the typical picture of post-infective encephalomyelitis with demyelinization most pronounced in the perivascular regions. "*Brachial neuritis*" (Hodges, 1940) has been described in four cases two to seven days after the appearance of the rash. Post-infective thrombopenic *purpura* such as occurs after scarlet fever (p. 1690) has been reported (Pitten, 1929; Gunn, 1933; Ackroyd, 1949).

Relapses were noted in 1 per cent. in a severe epidemic (Bennett and Copeman, 1940). They are rare in the ordinary mild form. *Second attacks* must be exceedingly rare if they occur at all.

Diagnosis.—Rubella is most likely to be mistaken for *measles*, *scarlet fever*, *glandular fever*, *pityriasis rosea*, and *maculo-papular rashes* due to toxins, allergens, drugs or serum. In measles the prodromal symptoms, with pyrexia and well-marked upper respiratory catarrh and conjunctivitis, usually last two to four days, and the rash is darker and more blotchy; Koplik's spots are pathognomonic. Nevertheless difficulty can arise with mild measles, especially sporadic cases occurring in summer and also with measles modified by sero-prophylaxis (p. 1731). In both these conditions Koplik's spots may be absent and post-measles staining inconspicuous. The scarlatiniform type of rubella can easily be confused with scarlet fever, especially after the rubella rash has faded from the face. The enlargement of the posterior cervical and occipital glands and the absence of tonsillitis, red papillated tongue and vomiting will be against a diagnosis of scarlet fever. The concurrence of rubella and tonsillitis, not a very rare event, may, however, be very puzzling. Dick tests, throat swabs and the Schultz-Charlton reaction are helpful in elucidating these conditions (p. 1692). In *glandular fever* a rash is relatively uncommon, limited in distribution (often to the trunk alone), appears after some days of malaise and glandular enlargement and persists for several days almost unchanged; the blood picture is one of relative and absolute mononucleosis; the Paul-Bunnell test is usually positive. *Pityriasis rosea* has a dimorphic rash: (1) small pink macules, (2) large oval patches up to an inch or more across, which change in colour in the centre from pink to fawn, accompanied by a fine scaliness, as the lesions grow. The distribution is usually on the trunk and proximal parts of the limbs. *Toxic and allergic rashes* are usually irregular in distribution, often on the extensor aspects of the limbs; the history is usually decisive.

Fourth disease (Dukes, 1900), a disease with characters intermediate

between those of scarlet fever and rubella is not now believed to be a separate entity. Some cases are the scarlatiniform type of rubella; some concurrent rubella and tonsillitis; some mild scarlet fever.

Erythema infectiosum (fifth disease, local rubella, Ringelröteln) is an epidemic disease occurring on the Continent and in the United States in spring and summer, principally in children between four and twelve years of age. The incubation period is five to ten days. Slight prodromata coryza, sore throat and malaise may occur. The first symptom, however, is usually the appearance of an erythematous rash of "butterfly" distribution on the cheeks, limited above by the temples and mesially by the naso-labial folds. The skin of the affected area is hot and swollen but not painful. After a day or two the rash appears on the proximal parts of the limbs, chiefly the extensor surfaces, and gradually creeps over the distal parts. The trunk is the last to be involved or escapes altogether. The rash is polymorphous, but large annular or gyrate patches are characteristic. These are similar to the variety of erythema multiforme known as erythema marginatum. The average duration of the eruption is eight to ten days. There is no adenitis, no desquamation, no complications, and usually little or no pyrexia. The blood picture shows a tendency to eosinophilia, and absence of plasma cells (Lawton and Smith, 1931). Were it not for the reported epidemics this disease might be considered a variety of erythema multiforme.

Exanthema subitum (sixth disease, roseola infantum, pseudo-rubella, das kritische dreitagefieberexanthem) is an eruptive disease resembling rubella in the appearance of the rash, posterior cervical glandular enlargement and febrile course, but occurring *exclusively in infants* between the ages of six months and two years. It was described by Zahorsky in 1910 and again by Veeder and Hempelmann in 1921. Most of the cases have been reported in the United States, the Continent and in and around London (Schlesinger, 1937). It consists of a sharp three-day fever associated with adenitis and mild pharyngitis and occasionally headache, drowsiness, rapid respirations and diarrhœa and vomiting in the younger infants; a critical fall of temperature on the fourth day and immediately *thereafter* a discrete macular rash on neck, shoulders and back, and later on abdomen and parts of the face and limbs. The rash fades in two or three days and the illness is over. It differs from rubella in the length of the prodromal period, the age incidence and its very slight infectivity. The blood picture may be useful in diagnosis—leucopenia with marked relative lymphocytosis and neutropenia.

Congenital malformations and rubella.—The exceptionally severe epidemic of rubella in 1940 brought to light in Australia, England and U.S.A. a most important connection between this otherwise trivial disease and such congenital malformations as *cataract*, *deaf-mutism*, *cardiac defects* and, possibly, bupthalmos, hypospadias, microcephaly and mental retardation. This whole problem has been fully discussed in an earlier chapter (p. 48).

Prognosis and treatment.—Rubella is a mild uncomplicated disease with rare exceptions which have been noted. The patient should be

kept in bed until the temperature is normal. No further treatment is usually necessary. Infectivity is short. Isolation for seven days is sufficient in nearly all cases provided that the temperature is then normal and the glands not tender, though they may still be enlarged. Quarantine of contacts is unnecessary. Pregnant women in the first few months of pregnancy should be protected from the infection by every possible means.

If they are known to have been exposed to the infection, convalescent rubella serum, or better, gamma globulin produced from it, should be obtained if possible and injected at the earliest moment after exposure.

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MUMPS

Synonyms.—Epidemic parotitis. *Fr.* Oreillons, *Ger.* Ziegenpeter, *Ital.* Strangulioni, *Sp.* Paperas, *Dutch* Bof.

Epidemiology.—The distinction between epidemic parotitis and other forms of inflammation about the parotid was well known to the Ancient Greeks and Romans, but subsequently became obscured until the infectious nature of mumps was again recognized in the eighteenth century. Hippocrates about 2,300 B.C. described an outbreak including the " lax, large diffused character " of the swellings and the accompanying orchitis. The disease is world wide in distribution, endemic in most centres of population, and particularly liable to occur in small outbreaks in schools, institutions and amongst recruits in the services.

Seasonal incidence is at its maximum in spring, and its minimum in late summer.

Age incidence is chiefly in the groups five to ten years and eighteen to twenty-five years. Infancy and old age are seldom attacked. The disease has occasionally occurred in the *new-born*, when the mother contracted mumps shortly before confinement. An erroneous diagnosis of mumps in infancy is common.

Sex.—There is an apparent higher incidence among males, at least after puberty.

Transmission is mainly by droplet infection probably from about four days before the onset of symptoms until the glandular swellings have subsided. The infective agent rapidly dies out when separated from the body, but recently contaminated clothing, or articles used by a patient, or even third persons may play a limited part in transmission. An important infective source is the mild or missed case in which no precautions are taken to prevent the spread of the disease. Henle and her associates (1948) showed by experimental spraying of children with virus, that many become "transient carriers" without clinical signs. The infectivity of mumps is comparatively low; susceptible contacts in children's wards, for example, often escape the infection although repeatedly exposed to it. Immunity conferred by one attack is nearly always permanent. Authentic second attacks are extremely rare but have occurred amongst young adults in sharp outbreaks.

Bacteriology.—Granata (1908), Gordon (1913) and Wollstein (1916) produced parotitis, orchitis and meningeal reactions by the injection of sterile salivary filtrates into animals by various routes. They all concluded that mumps was caused by a filterable virus. This was confirmed by Johnson and Goodpasture (1934) and by Findlay and Clarke (1934) who reproduced the disease by injection of the filtered material into the parotid duct of monkeys. Enders and his collaborators (1945) demonstrated specific antibodies in the blood serum in infected monkeys and in the natural disease in man. The antibodies seem to be attached to the gamma globulin fraction of the serum. They can be demonstrated by a complement fixation reaction and by a skin test of the sensitivity type. They are present in primary mumps meningo-encephalitis in the absence of clinical evidence of salivary gland involvement. The antigen for these tests was obtained from a monkey's infected parotid. Injection of the formolized antigen subcutaneously in the monkey produced a certain degree of active immunity. Later Habel (1945) cultivated the virus on developing eggs by injecting into the embryo a suspension of infected monkey parotid. This method provides a more reliable antigen than monkey parotid suspension for the complement fixation reaction and skin tests. Leymaster and Ward (1947) produced culture virus by direct inoculation of saliva into eggs. The virus of mumps was found by Habel to be inactivated by a temperature of 55° C. for twenty minutes, by 0·2 per cent. formalin at 4° C. in twenty-four hours, by 1·5 volumes of ether, or by an exposure of 0·28 seconds to ultra-violet light. The work of Henle (1948) established the presence of virus in sub-clinical salivary gland invasion and that the period of infectivity of such cases was longer than in the clinical cases. The virus exhibits *neurotropism*. The infection of mumps occasionally presents itself in the form of meningitis or encephalitis, and a cyto-chemical reaction in the meninges is common in uncomplicated cases. It was suggested by Dopter (1910) that mumps is primarily a virus infection of the nervous system and the parotitis secondary, the organisms being eliminated by the salivary glands, as in

rabies. This would seem to be disproved by Henle's work, however, which showed that orchitis could occur as long as nine or ten days after the virus had disappeared from the saliva, and that virus did not reappear in the saliva. Neurotropism is rarely seen in children.

Pathology.—There is little knowledge of morbid anatomy since death from mumps is rare. Rocchi (1933) carried out biopsies on ten cases of mumps and found a *small-celled infiltration of the interstitial and peritubular tissues* of the parotid. Cytoplasmic inclusions were later found in the acinar cells. By catheterization of Stenson's duct he also found that salivary secretion was often abolished and always diminished, and when present contained polymorphonuclears, lymphocytes, glandular and epithelial cells; the calcium and chloride content was increased for two weeks from onset. In mumps orchitis, according to Stengel (1936), the essential pathological process is a parenchymatous sclerosis. In pancreatitis complicating mumps the organ is congested and œdematous. So far no interstitial lesions have been found.

FIG. 580.—MUMPS, ABOUT FOURTH DAY OF SWELLING.

Blood changes.—As a general rule the blood shows a moderate or slight lymphocytosis, although not uncommonly, at onset, the leucocyte count is normal or there is a leucopenia. At the onset of orchitis some observers have found a polymorphonuclear leucocytosis. The blood sedimentation rate is normal except in orchitis.

Symptomatology.—The incubation period is most commonly seventeen to nineteen days, the extreme limits probably being twelve to twenty-six days. In most cases the first symptom is pain in the region of one or other parotid, young children often complaining of "toothache." Actual enlargement of one or other parotid is, however, not infrequently the first indication of the disease. Prodromal symptoms of fever, with fretfulness, headache, vomiting, and sore throat, are usually absent, but occasionally occur even up to four days before the swelling is observed. Occasionally, but rarely in children, the presenting sign at onset is not a swelling of a salivary gland, but orchitis, meningitis, encephalitis or pancreatitis. Both parotids may enlarge simultaneously, or, more frequently, one a day or two after the other. Not infrequently one or both submaxillary salivary glands are affected, with or without parotid enlargement. Sublingual gland enlargement is not common, but it may be the only sign of the disease, in which case the diagnosis is easily missed. In all cases of suspected mumps it is well to look under the tongue for swelling of the sublingual area. Other early signs to be looked for, but not always

present, are : (1) reddening and œdema of the papilla or orifice of Stensen's duct, and (2) *Hatchcock's sign*—tenderness on pressure just beyond the angle of the jaw, on running the finger towards the angle under the mandible.

The swollen parotid fills up the recess between the mastoid process and the ascending ramus, whilst the part of the gland overlying the masseter muscle is so elevated that its outline is easily palpated. Local pain and tenderness is usually moderate or slight, but there is always some pain on mastication. In severe cases, certain mechanical effects of the swelling may be observed, *e.g. trismus* and temporary *deafness* from œdema of the meatus. The skin overlying the swollen parotid is shiny and flushed. The saliva is diminished and the mouth becomes dry and foul. Enlargement of the *spleen* has been noted but is inconstant. The temperature may be normal throughout but more frequently ranges from 99° F. to 103° F. for three to five days. There is little constitutional disturbance. Fauces, buccal mucosa and palate are normal. The duration of the swelling ranges from a few days to three or four weeks and occasionally longer. Complete resolution is the rule : suppuration or chronic enlargement is exceedingly rare. After subsidence of the parotid swellings, the attack is usually at an end, but submaxillary and sublingual glands may become involved either simultaneously or at a variable time later.

Complications.—*Orchitis* is the most important and frequent complication. It usually affects one testis, with or without the epididymis, but occasionally both testes are involved. It is very rare before puberty. Stengel (1936) could find only five cases reported before the twelfth year of age. It is commonest in sexually active young adults. It usually occurs about a week after onset, but may be earlier or later and may even be the first and sometimes the only sign of the disease. The pulse and temperature are raised and the patient is anxious and ill. The testicle and epididymis are swollen, painful and tender. In severe cases there may be vomiting, delirium and prostration ; other complications, *e.g.* meningitis, encephalitis or pancreatitis may be concurrent. The condition subsides in a week or ten days. Atrophy of the testis as a sequela of mumps orchitis is almost always unilateral and incomplete. Impotence and feminism as sequelæ are exceedingly rare. The incidence of sterility following mumps is still doubtful and has probably been overemphasized. Bénard (1931) was unable to find azoospermia even after double orchitis. *Oöphoritis* and *mastitis* occur in the female but are much less common than orchitis and usually mild.

Pancreatitis is much more rarely diagnosed than orchitis. Like the latter it occurs in the acute stage or in convalescence or may even be a presenting and sometimes the only sign. The symptoms are pyrexia, acute pain and tenderness and sometimes rigidity in the upper abdomen, with vomiting, anorexia, constipation and diarrhœa. The stools contain excess fat, and the urine may contain sugar in addition to ketone bodies. Palpation of the epigastrium may reveal a swollen pancreas. Recovery is the rule. Farnam (1932) collected 119 cases of which only one was fatal. It has been suggested that some cases of *diabetes* may result from

the pancreatitis of mumps. Couronne (1927) collected nine cases of diabetes following mumps. More recently Cole (1937) described three cases under his own care of severe diabetes in children and referred to five others. Only in three of Cole's eight cases were there any definite abdominal symptoms during the attack of mumps. This may mean that pancreatitis may sometimes be a silent complication of mumps. On the other hand the evidence does not exclude a mere fortuitous association between mumps and diabetes. Investigation of infectious diseases preceding diabetes fails to confirm this idea (White, 1932).

Nervous system and sense organs.—Complications involving these are rare in children. A *meningeal reaction* without symptoms has been shown by serial lumbar punctures throughout the disease to be relatively common even in uncomplicated mumps (Tocmann, 1920-21). In this series the spinal fluid, usually at an early stage, sometimes later, showed increased lymphocytes, protein and glucose with diminished chlorides. In children, according to my observations, a single lumbar puncture in the acute stage yields normal fluid in the majority of cases. Clinical *meningitis* is certainly rare, except in war-time or other severe epidemics, when it may appear either as a presenting sign or about the fifth day after onset. Thus out of 234 of the more serious cases of mumps admitted to hospital in an epidemic among young soldiers, Frankland (1941) found no less than 30 per cent. to have signs and symptoms of meningeal involvement. The symptoms are pyrexia, headache, nausea, vomiting, bradycardia and neck rigidity. Kernig's sign is usually present. Symptoms subside after three to five days. The spinal fluid contains up to a few hundreds of cells, the majority of which are lymphocytes. This condition would be indistinguishable clinically from other forms of benign aseptic meningitis, but for the presence of associated mumps or orchitis. Mumps *encephalitis* seems to be at least of two kinds : (1) the post-infective perivascular demyelinating type arising a few days after onset (p. 1728) and (2) the type commencing about the time of onset of the glandular swelling, and possibly due to viral action on the neurons themselves.

A case of the latter type was seen in December, 1936, a child aged four years who became unconscious just as the parotids were beginning to enlarge and next day developed convulsions and left hemiplegia with extensor plantar response. The convulsions lasted three days, the coma six days and the hemiplegia eight days. Recovery was thereafter rapid and complete. The spinal fluid was normal.

The prognosis in mumps encephalitis is good.

Peripheral neuritis is a rare complication. It may be a polyneuritis chiefly affecting the extremities ; or cranial nerves, particularly the facial, optic, auditory or oculomotor may be involved. It has been suggested that, in view of the meningeal reaction in mumps, neuritis is likely to be caused by meningo-radiculitis rather than by a lesion of the peripheral nerve endings. Rapid recovery is usual, with two exceptions, the optic and auditory nerves, where atrophy is apt to follow with permanent blindness and deafness (Butler and Wilson, 1937). *Œdema of the larynx* is an uncommon complication associated with severe submaxillary mumps.

It may require tracheotomy. *Œdema of the tongue* and of the anterior chest wall (Radin, 1918) may occur in connection with sublingual mumps. Very rare complications are *iritis* and *irido-cyclitis* and *phlebitis* of the lower limb secondary to orchitis. The prognosis in these is good.

Diagnosis.—Acute parotitis in children is nearly always a sign of mumps. Septic parotitis is rare in children but may occur when the mouth is dry and becomes foul, *e.g.* after typhoid, scarlet fever, coma from any cause, or surgical operations. It soon becomes suppurative and pus can be seen oozing from Stensen's duct. This is never seen in mumps. An important point in diagnosis of parotid swelling is to palpate the outline of the part of the parotid overlying the mandible, and also the space between ear and jaw, where the posterior border of the ascending ramus cannot as a rule be defined because of the swollen parotid. This procedure will eliminate other swellings such as *pre-parotid lymphadenitis*, and most important of all, *bull-neck toxic diphtheria* (p. 1704). In the latter case an erroneous diagnosis of mumps is a tragedy since it leads to delay which is often fatal. Other conditions requiring differentiation, but rarely seen in children, are toxic parotitis, *e.g.* from mercury and iodides, *salivary calculus* (unilateral), *tumours* (unilateral), and the *uveo-parotid syndrome* (chronic). The occurrence of solitary submaxillary or sublingual mumps must be borne in mind.

Serum diastase in mumps is above the normal figure of 60 to 180 units per c.cm. in about three-quarters of the cases (Zelman, 1944). It is unknown whether this increase in diastase is due to the salivary lesions or to silent pancreatitis. When pancreatitis can be diagnosed clinically, the serum diastase values are very high and may reach 1,000 units per c.cm. An abrupt rise in the diastatic index offers confirmatory evidence when pancreatitis is suspected clinically.

Prognosis.—This is almost always favourable, even in complicated cases.

Prophylaxis.—The infective period probably extends from the end of the incubation period (possibly four days before onset of symptoms), until the last salivary gland to enlarge shows signs of abatement. In most cases this is little more than a week from onset (Henle *et al.*, 1948).

Isolation should be maintained until the swelling of the gland affected has subsided except in cases of prolonged subacute enlargement due to mild sepsis. The minimum period of isolation is usually two weeks.

Quarantine of contacts is not generally practised owing to the long incubation period and the relatively low degree of infectivity. Thus 37·7 per cent. of primary cases of mumps in boys' boarding schools did not give rise to secondary cases (M.R.C. Report, 1938). Exposed children may be kept under observation for early signs of the disease from the twelfth to the twenty-eighth day after exposure. Complete and rigid segregation is impracticable and possibly not desirable since it is an advantage for boys at least to have mumps before puberty rather than after.

Convalescent serum has so far been disappointing in the prophylaxis of mumps. Johnson and Goodpasture (1936) failed to protect monkeys by convalescent serum against intra-parotid injection of the

virus. In human contacts, the use of serum has given inconclusive results. Although there may be some success, failures will certainly occur. Beeson *et al.* (1944) found the attack-rates in an inoculated group of recruits and in controls not significantly different. A disadvantage of the convalescent serum in this experiment was that in a considerable number of cases hepatitis developed in the inoculated.

Gamma globulin prepared from mumps convalescent serum has been used with success in the prophylaxis of orchitis. A dose of 20 c.cm. given to adolescents at the onset of the parotitis significantly reduced the incidence of orchitis as compared with that in uninoculated controls (Gellis *et al.*, 1945). Stilbœstrol 2 to 4 mgm. daily has been used prophylactically for seven days from onset in young adults with the same object.

Treatment.—The patient should be kept in bed during the period of parotid swelling. In mild cases ordinary diet can be given after the first day or two. In severe cases, semi-fluid diet, and in trismus feeding through a straw may be necessary. The toilet of the mouth is important after all meals. Glycerine of belladonna local applications may be made to swollen parotids or testes. A suspensory bandage should be provided in all cases of orchitis, and morphine may be required to relieve the pain. Stilbœstrol 5 mgm. daily has been used for orchitis with the idea of inhibiting testicular function (Hoyne, Diamond and Christian, 1949). This treatment is difficult ot evaluate.

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GLANDULAR FEVER

Synonym.—Infective mononucleosis.

Glandular fever is an acute infectious disease, most variable in its manifestations, but characterized principally by glandular enlargement, irregular, mild intermittent fever, lymphocytosis with a high proportion of abnormal mononuclears and heterophile antibody in the blood (positive Paul-Bunnell reaction). It was first described by Pfeiffer in 1889.

Epidemiology.—The disease is generally of low infectivity and occurs sporadically and in limited local epidemics. It has often been treated in general wards without spread of the disease. Most of the reported epidemics have occurred in hospitals and institutions. Occasionally, the disease has a high infectivity, *e.g.* in one epidemic among young soldiers in a hospital, where no less than 97·9 per cent. of 296 persons investigated had a positive Paul-Bunnell reaction and a typical blood picture, and as many as 40 per cent. of them presented clinical symptoms of glandular fever (Halcrow, 1943). Undiagnosed mild and latent cases are probably quite common in epidemics.

Most cases occur in spring and autumn. It has been considered mainly a disease of children. Tidy and Morley (1921) estimated that 85 per cent. of epidemic cases occurred in children under twelve. The disease is, however, not infrequent among adolescents and adults. Boys are rather more frequently attacked than girls.

Bacteriology.—The causal agent is unknown. It is at present assumed to be a filterable virus or a number of closely related viruses. Attempts at experimental transmission of the disease have mostly failed. Bang (1942) injected filtered material by various routes into monkeys but did not succeed in transmitting the disease. Other workers (Stannus and Findlay, 1939; Wising, 1942) have had suggestive results with single transmissions. It should, however, be stated that a short motile gram-positive bacillus, *Listeria monocytogenes* which grows best at 23° C., has been cultured from the blood of cases of glandular fever on three occasions since 1929 (Webb, 1943). The evidence must be considered inconclusive at present since agglutinins to this organism are not present in significant titres in the blood of patients with glandular fever, nor do rabbits injected with the organism give positive Paul-Bunnell tests. No strong claim can be put forward at present for any particular causal agent.

Incubation period.—This may range from five to fourteen days and is generally about eleven days.

Symptomatology.—Tidy (1934) described a glandular, febrile and anginose type, the last being much rarer than the others. Other types might be added, *e.g.* the cerebral and hepatic. But so diverse are the clinical features, that Bernstein (1940) in his comprehensive review,

remarked "On a modest scale infectious mononucleosis can be said to resemble syphilis in virtue of its ability to simulate so many other diseases." Accordingly only a general descriptive outline can be attempted here. The initial symptoms are usually those of vague constitutional upset, but may be sudden with chills and high fever. Many cases are so mild that they may pass unrecognized. The febrile stage lasts usually from one to two weeks, but may be shorter, and, on the other hand, relapses may prolong the period of illness with occasional fever but little constitutional disturbance for as long as six months. Subjective recovery is seldom postponed for more than a month from onset, although the lymphadenopathy may last much longer. General features of the early stage of the illness include malaise, headache, vomiting, abdominal pain (which may simulate appendicitis), vertigo, constipation or diarrhœa, conjungtivitis, photophobia and epistaxis. Special features are as follows.

Glandular enlargement is probably the most common single feature of the disease. It may be widespread but is much more commonly confined to the neck, especially the sternomastoid and submaxillary regions, first on one side and then on the other. The glands may rapidly reach the size of a plum or even an egg and the neck become stiff from the swelling. The glands may enlarge at the beginning of the illness or, more commonly, only after pyrexia has lasted for some days or even weeks. They are tense, elastic, fleshy to palpation and slightly tender. Groups of glands other than those in the neck which may be involved include the axillary, the inguinal and the epitrochlear. The glandular enlargement is often intermittent over a long period.

Sore throat.—The tonsils are usually enlarged and sometimes also the post-nasal adenoid lymph tissue (Kilham and Steigman, 1942). Some cases (anginose type) have a greyish white patch of exudate, slough, or even membrane in the fauces, from which Vincent's organisms, streptococci diphtheroids and other mouth organisms may be isolated.

Conjunctiva.—A proportion of cases show hyperæmia of the conjunctiva, sometimes with palpebral œdema, possibly the result of pressure from enlarged glands.

Spleen and liver.—Slight splenomegaly or, at least, tenderness in the splenic region is present in about half the cases. Hepatomegaly is very rare.

Exanthem.—Rashes are uncommon in children, but occur in an appreciable proportion of cases in adolescents. They are purplish in colour, of fine macular or scarlatiniform type, presenting often a fine mottled appearance, and are usually limited in distribution, mainly to the trunk. A sparse petechial rash on the limbs has occurred in rare cases. *Enanthem*—red papules may appear on the palate, or even petechiæ on the buccal mucosa, the latter sometimes associated with hæmaturia or epistaxis (Kilham and Steigman).

Jaundice is not common, but some cases have frank jaundice and some have a raised icteric index without clinical symptoms. The jaundice is obstructive in type with direct positive van der Bergh reaction. It has been attributed to pressure of glands on biliary ducts, or, alternatively,

to hepatitis. Not enough liver biopsies have yet been done to determine this point.

Thoracic and abdominal symptoms.—Pain in the chest and cough may be prominent symptoms, probably due to enlarged tracheo-bronchial glands. Vomiting, transient diarrhœa and abdominal pain may be similarly due to pressure of enlarged glands.

Meningitis and neurological signs.—Rarely neck rigidity and other signs of meningeal irritation warrant lumbar puncture. In such cases the spinal fluid usually shows a mild pleocytosis and protein increase ; rarely there are encephalitic signs.

Tidy (1946) raised the question whether " benign lymphocytic meningitis " might not be one of the neurological manifestations of glandular fever. He pointed out that the clinical symptoms, course, prognosis, and changes in the cerebro-spinal fluid are identical in the meningitis associated with the two conditions. In the presence of such neurological symptoms, glandular fever can only be excluded by specific and repeated examinations, and these have rarely been made in cases recorded as benign lymphocytic meningitis.

He summarized existing knowledge of the neurological manifestations of glandular fever. The symptoms are not only meningeal, but may be encephalitic or neuritic. They may develop before or after the usual characteristic features of glandular fever. During the period of neurological symptoms, the blood count may be normal or polynuclear leucocytosis may be present.

Blood picture.—A cardinal sign of the disease, usually developing a few days after onset, is an absolute and relative lymphocytosis with a high percentage of monocytes or abnormal lymphocytes. The chief characteristic of the latter is their variability (Bernstein). They are of the size of large lymphocytes with basophilic cytoplasm and deep coarsely staining or fenestrated nuclei of irregular shape. The polynuclears may be normal or decreased. There is no appreciable change in the red cells. At the onset of the severe types the blood count may show a polymorphonuclear leucocytosis, or may be normal, or even leucopenic.

Paul-Bunnell reaction.—Another cardinal change in the blood which can be measured is the presence of heterophile antibody in high titre (agglutinins of sheep red cells). An agglutination titre of 1 in 80 is believed to be diagnostic of glandular fever, provided that recent injections of horse serum can be excluded. The Barrett modification of this test differentiates heterophile antibody resulting from injection of horse serum from that of glandular fever. The latter is absorbed by ox erythrocytes but not by guinea-pig kidney, whereas the horse serum antibody is absorbed by both. If the Barrett absorption test is positive, the Paul-Bunnell test in a titre of 1 in 40 or above is considered diagnostic of glandular fever.

Pathology.—The *lymph glands* show a great hyperplasia of lymphoid and reticulo-endothelial cells (Pratt, 1931). The gland architecture is usually maintained and the abnormal lymphocytes found in the peripheral blood can be demonstrated throughout the glands (Gall and Stout, 1940). These changes are not diagnostic, but biopsy of a lymph gland would usually differentiate between infectious mononucleosis and more serious

conditions such as lymphatic leukæmia and lymphadenoma. The bone-marrow shows no great change in some cases, and in others an increase in plasma cells and abnormal lymphocytes (Vogel and Bassen, 1939). From extensive autopsy and biopsy material Custer and Smith (1948) showed that in severe cases lymphocytic and reticulo-endothelial hyperplasia might destroy the architecture of glands, and invade the trabeculæ and capsule of the spleen making that organ liable to rupture.

Complications.—It is difficult to separate symptomatology from complications, but hæmaturia, serous meningitis and jaundice may be considered the chief complications. Suppuration of the glands is exceedingly rare. A relapsing course of the disease over several months is not uncommon, but second attacks do not seem to be recorded.

Diagnosis.—The *glandular* type may be confused with *mumps*, *acute lymphoid* or *monocytic leukæmia* and *lymphadenoma*. Mumps should be excluded by the absence of salivary gland enlargement, although the pre-parotid lymph gland, if enlarged, may be confusing. In the leukæmias, constitutional symptoms are severe and there is anæmia in addition to leucocytic changes. Swelling of the gums, stomatitis, purpura, hæmorrhages, weakness and fever all tend to be much more severe in acute leukæmia. Bone marrow examination would probably be conclusive. In lymphadenoma, the affected glands are not tender and there is no lymphocytosis. The *anginose* type may be mistaken for *diphtheria*, *Vincent's angina* or *agranulocytic angina*. Throat swabs, blood counts, and the Paul-Bunnell test in addition to the clinical appearances should differentiate glandular fever from diphtheria and other anginas. Vincent's organisms may play a secondary rôle in glandular fever, but the two conditions should be differentiated by the symptomatology and blood tests. *Secondary syphilis* with mucous patches in the fauces and a rash may give rise to difficulty, especially as *the Wassermann reaction may be temporarily positive during the course of glandular fever* (Radford and Rolleston, 1930). The *febrile* type of glandular fever with rash may be confused with *typhus* or *typhoid fevers*, *measles or rubella*; and when jaundice is present with *infective hepatitis*. Here again the symptomatology, blood picture and Paul-Bunnell test should generally be conclusive. Infective hepatitis has a much longer incubation period.

The Paul-Bunnell reaction occasionally does not become positive for several weeks in glandular fever, or it may even be negative throughout. Paul (1941) stated his belief that the test is nearly always of positive diagnostic value (provided one can exclude serum disease) in a titre of 1 in 64 and of suggestive value in a titre of 1 in 32, but *that a negative test does not eliminate the diagnosis*. In suspected cases if the reaction is negative, the test should be repeated over several weeks.

Acute infectious lymphocytosis.—This condition, mainly found in children, was first described by Smith (1941). The clinical manifestations are mild, and of short duration, *e.g.* those of upper respiratory tract infection, slight axillary adenopathy, pains in the side and sometimes a maculo-papular rash on trunk and limbs. There is a leucocytosis of 16,000 to 60,000 per c.mm. with 50 to 80 per cent. of *normal mature*

lymphocytes. The Paul-Bunnell test is negative. The lymphocytosis lasts for two to three weeks and the disease is then over. Smith (1944) considers the disease to be both infectious and contagious and to have an incubation period of twelve to twenty-one days. Lorenz and others (1946) state that thirty-two cases have been reported since 1941. They discuss the possibility of the disease being: (1) an atypical kind of infectious mononucleosis or (2) pertussis without the usual cough, *e.g.* in inoculated subjects. They conclude, however, that it should be regarded as a separate disease entity.

Treatment.—The prognosis of glandular fever is almost invariably favourable without special treatment. Isaacs (1948) has described cases with low blood pressure, fatigue, splenomegaly and hypoglycæmia persisting up to four years. Convalescence may, however, be protracted. Treatment is purely symptomatic. The patient is usually isolated for at least two weeks although there is no evidence that this limits the spread of the disease. Quarantine of contacts is unnecessary.

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ERYSIPELAS

Synonyms.—*Fr.* Érysipèle. *Ger.* Rotlauf. *Ital.* Risipola. *Span.* Erysipela.

Epidemiology.—Erysipelas is one of the hæmolytic streptococcal acute fevers. It is not due to a specific *streptococcus erysipelatis*, as was formerly supposed, but to the action of any of the human pathogenic types of hæmolytic streptococcus (see scarlet fever, p. 1679). Nor is there any evidence that the typical inflammatory lesion of the skin is due to the erythrogenic toxin of the hæmolytic streptococcus. It is not blanched by streptococcal antitoxin. It is not a toxic effect, but the

result of the growth of the organisms themselves. Erysipelas is common in infancy amongst both Dick-negative and Dick-positive subjects, but its main age incidence is in middle-aged and old people who are generally Dick-negative. The hæmolytic streptococcus enters the skin through a visible or invisible breach. In the former category are included gross lesions like surgical wounds, old septic sinuses, ulcers of the leg, septic stump of the umbilical cord in the new-born, vaccination pustules, and also small cracks, fissures and scratch marks in the skin, around the nares, pinna, eye and elsewhere. In many cases, however, the breach of the skin which forms the portal of entry is not visible to the naked eye. A visible primary focus of infection in the skin is found far more frequently in erysipelas of the trunk and extremities than in facial erysipelas, but even in the facial type, it is found in about half the cases. The remainder are probably infected from purulent, inflammatory or latent infections of the mucosa of the upper respiratory tract, accessory sinuses, ears or eyes, which are commonly found to precede or accompany facial erysipelas (Flensborg, 1942).

Erysipelas occurs mainly but not exclusively in cold weather and in cold damp climates. Its incidence corresponds generally with that of hæmolytic streptococcal infections. It formerly occurred in epidemics, *e.g.* in overcrowded hospitals and institutions, but is now chiefly a sporadic disease.

Pathology.—The inflammatory process includes the whole skin of the affected area. Hæmolytic streptococci are found in the lymphatic spaces below the epidermis, especially in the area just beyond the advancing edge of the lesion. The skin is red, œdematous and infiltrated with polymorphonuclears and mononuclears : although the vessel walls are involved, thrombosis and hæmorrhages are not common. As the lesion spreads, the organisms in the area behind die out, and the inflammation subsides. Cultures from the blebs which form in the epidermis in severe cases are usually sterile. Regional lymph gland enlargement is generally not marked. Occasionally the infection extends more deeply into the cellular tissue below the skin, thus producing simultaneous erysipelas and cellulitis.

Symptomatology.—The incubation period is variable, generally one to seven days after infection. The onset is abrupt with shivering, headache, generalized pains, vomiting and pyrexia. In children convulsions may occur. Within a few hours the local lesion appears at the site of inoculation. The skin feels " tight " : it is uniformly red and tensely infiltrated so that it becomes hard, inelastic, raised, shiny and may contain blebs on its surface. The spreading edge bevels down to the adjoining normal skin and is well demarcated from it. This is a characteristic feature of erysipelas. In facial cases the lax connective tissue of the skin of the eyelids may swell so greatly that the eyes become closed. Similar swelling occurs in the vulva and scrotum and in all these situations spread of the inflammation is rapid. In situations where the skin is firmly attached, as at the chin, the spread is retarded and may be halted. *Constitutional disturbance* varies considerably but is often profound, with

restlessness, delirium, prostration and semi-coma and even the typhoid state. Delirium is especially severe in erysipelas involving most of the scalp, and may be associated with violence and suicidal tendencies.

Course.—In the untreated disease, the inflammation generally spreads for three to six days with increasing toxæmia, and then subsides in the oldest part of the lesion while the spreading edge may still advance for a time. Infrequently the lesion may continue to advance for two to three weeks until the greater part of the body has been covered (*erysipelas migrans*). Desquamation, pigmentation and some thickening of the skin remain for a time after the acute stage, especially in severe cases with bullæ.

Erysipelas neonatorum has in the past had a mortality of about 50 per cent. It is usually associated with an umbilical slough. The lesion tends to spread over the abdomen and thighs, to cause sloughing of the skin around the umbilicus, infection of the umbilical vein, followed by multiple abscesses in the liver and general peritonitis. This dreadful sequence of events can now be rapidly controlled by chemotherapy. Occasionally the point of entry of the hæmolytic streptococcus is in the napkin area, and in this type there is also danger of sloughing and septicæmia. Erysipelas of infants, after the first month of life, is serious but not so fatal as in the new-born. The most common points of entry are abrasion in the napkin area, a circumcision operation wound and a vaccination pustule. In the infant's soft skin the spread of inflammation is rapid, the œdema intense, and small hæmorrhages are apt to occur. The accompanying toxæmia is severe and if the process is not promptly checked, the course is rapidly downwards with septicæmia, dehydration, wasting and death.

Complications.—*Erysipelo-cellulitis*, which occurs more in the extremities than in the face, has already been noted. *Localized abscesses* of the subcutaneous tissue occasionally occur from secondary infection with staphylococci. *Necrosis* and *gangrene* of the skin are prone to occur in the genital and inguinal regions due to obliteration of the blood supply by pressure of the œdema or thrombosis of the vessels. Streptococcal *septicæmia* is uncommon except in very young infants. Streptococcal *meningitis* spreading directly from the inflamed scalp is fortunately very rare. Erysipelas of *mucous membranes* has been postulated as a spread from adjacent skin affecting buccal mucosa, fauces, and larynx, but this is difficult to distinguish from catarrhal inflammation of these parts. *Broncho-pneumonia* is rare in children but more common in the aged. *Relapse and recurrence* in erysipelas were, until recent years, exceedingly common. Recurrences or re-infections are still of frequent occurrence when there is a persisting focus of infection such as suppuration in the maxillary sinus or a fungating carcinoma. In the great bulk of cases, however, in which no persistent endogenous septic focus can be demonstrated recurrences have been considerably reduced since the introduction of chemotherapy.

Diagnosis.—The raised, hot, uniform erythema with its definite spreading edge usually makes diagnosis easy. When the nose is involved

the erythema is usually across the upper part or bridge. If the point of the nose is inflamed and especially if the erythema presents no well-defined edge, staphylococcal inflammation spreading from a boil or focus in the nares should be suspected. As this is a most dangerous lesion which may lead to cavernous sinus thrombosis, it is essential to treat it at once with penicillin if it is suspected on clinical grounds and confirm the diagnosis without delay by swabs and blood cultures.

Prognosis.—The prognosis in all forms of erysipelas, all over the world, has been strikingly improved by sulphonamide therapy. Thus, case fatality rates for many years prior to 1938, averaging 12 to 14 per cent. in Cook County Hospital, Chicago, 7 to 9 per cent. in Ruchill Hospital, Glasgow, and 6 to 7 per cent. for England and Wales generally, all became reduced to the common figure of about 2 per cent. in 1938, and have since fallen to an even lower level (*Med. Annual*, 1941). This acute fall synchronized exactly with the use of sulphonamide preparations and could hardly be due to any other factor. Now, the main factor in prognosis is early and adequate chemotherapy.

Treatment.—The sulphonamides were at first so strikingly effective in erysipelas that they rendered obsolete all the older methods of treatment, including local applications, ultra-violet light and streptococcal antitoxin. Any of the standard sulphonamides, even sulphanilamide, the weakest, when first employed in the early years of the sulphomanide era was generally effective. It is best, however, to use the newer sulphonamides, *e.g.* sulphathiazole or sulphadiazine, and if results are not quickly obtained (owing to sulphonamide-resistant streptococci) to combine it with penicillin. The dosage of sulphonamides is as for severe infections in infants ($\frac{1}{2}$ gramme four-hourly) and as for moderate infections in older children (three to ten years. $\frac{1}{2}$ gramme four-hourly; eleven to fifteen years, $\frac{3}{4}$ gramme four-hourly). After three days the dosage is reduced and after six or seven days can usually be stopped. In order to avoid relapses it is well to continue the drug or drugs for two days or so after the redness and swelling have subsided. Alkalis and liberal fluids must also be given in accordance with the rules of sulphonamide therapy. In facial cases irrigation of the eyes is often required. No local covering is usually required. Irritation and itching may be relieved by painting with calamine lotion, with 10 per cent. ichthyol or a lotion containing solutions of lead subacetate and of coal tar. Sedatives and analgesics may be required for one or two nights in severe cases.

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TYPHOID FEVER

Synonym.—Enteric Fever, *Fr.* Fièvre typhoide, dothiénenterie; *Ger.* Unterleibstyphus; *Ital.* and *Sp.* Tifo; *Dutch* Buik-typhus.

Introduction.—Typhoid fever is a general infection caused by the

group of organisms now known as *Salmonella typhi* (formerly *Eberthella Typhosa* or *B. typhosus*). It is characterized clinically by a gradual onset, continued fever, intestinal disturbance, enlarged spleen and an eruption of rose spots. Pathologically there is early bacteræmia, hyperplasia and ulceration of lymphoid tissue of the intestines, swelling of the mesenteric glands and spleen and toxic parenchymatous changes in the heart, liver, kidneys, lungs and other organs. In children it tends to pursue an atypical and often mild course with tendency to relapse; certain cases in infants, however, simulate enterocolitis, pneumonia or meningitis, and amongst this group the death-rate is high.

Typhoid fever was first described in the seventeenth century, recognized as infectious by Bretonneau (1818), distinguished from typhus fever in U.S.A. by Gerhard (1837), and the infection traced to fæcal contamination by Budd (1873). The causal organism was discovered by Eberth (1880), and the agglutination test for diagnosis by Widal (1896). The bacteriæmia was first demonstrated by Schottmüller (1901). Anti-typhoid inoculation was first practised by Wright (1896).

Epidemiology.—The typhoid bacillus enters the body chiefly by ingestion of water or food which has been contaminated by fæces or urine of cases of the disease or carriers. In rural areas water is most frequently contaminated by seepage of sewage from cesspools into shallow wells and water courses. But even the pure water supplies of towns are liable to occasional contamination in the reservoirs or wells by an unrecognized urinary or fæcal carrier, or in the pipes by leakage from near-by soil pipes or sewers. Foods which are most readily contaminated include milk, cream, ice-cream, butter, cheese, cooked meat, salads, fruit, and shellfish such as oysters, mussels, cockles, whelks and winkles. Shellfish acquire the bacilli when they are reared in sewage-contaminated waters or steeped in such water after removal from their culture beds. The typhoid bacillus can live in water for some weeks and in shellfish as long as thirty-four days. Shellfish eaten raw, *e.g.* oysters, should always be immersed in at least three baths of chlorinated water before being exposed for sale. Salads and fruit are rarely contaminated except in districts and countries where human excreta are used as manure. Food may be contaminated with excreta indirectly through the agency of flies or by means of the infected hands of carriers or of attendants on cases of typhoid fever. In most cases food is infected by unrecognized carriers.

In a room or ward in which typhoid fever is nursed many fomites become infected, *e.g.* telephone, door-handle, trays, as well as blankets, sheets and patients' clothing. The danger of infection of attendants from these sources is real. During the period 1909–14, no less than eighty of the staff of the M.A.B. fever hospitals, including sixty-five nurses, developed typhoid fever (Rolleston and Ronaldson, 1940). This danger was mitigated only when it became the practice to inoculate with T.A.B. vaccine all staff exposed to enteric infection. The latter includes not only cases of typhoid and paratyphoid fevers, but typhoid abscesses long after the acute stage has passed, and carriers.

Incidence.—In Britain the incidence has greatly diminished, since the introduction of pure water supplies to the towns and larger villages following the cholera epidemics of the early nineteenth century. The downward trend in incidence was greatly accelerated by the abatement of the grosser sanitary nuisances which followed the Public Health Act of 1875, and again by the reduction of flies associated with the replacement of horse by motor transport and by improvement of conservancy methods, in the first two decades of this century. Since then there has been a further steady decrease, only interrupted in certain years by the occurrence of water-borne or milk-borne epidemics due to unrecognized carriers. In the six war years 1939-44 annual notifications of typhoid fever (excluding paratyphoid) varied from 356 to 1058 : and the deaths from 45 to 90 and since then there has been a further decline.

Age and sex.—The disease is most common in adolescents and young adults, but no age from infancy to old age is exempt. Congenital typhoid may occur in an infant born of a mother suffering from the disease. The incidence in children under five years may be underestimated owing to its atypical clinical course. In milk-borne epidemics the incidence among children is especially high. In the M.A.B. hospitals from 1894 to 1914 admissions for typhoid fever according to age-groups in children were : under 5 years, 455 : 5 to 10 years, 1,484 ; 10 to 15 years, 2,079. The sexes were almost equally affected (Rolleston and Ronaldson, 1940).

Season.—It is a disease mainly of late summer and autumn with the maximum incidence in October.

Geographical distribution.—This is world-wide. Prevalence appears to be greatest in areas of poor sanitation in temperate zones. In warmer climates the disease may be latent among the natives who acquire immunity in varying degrees. Europeans in India, China, Malaya, for example, are much more susceptible to the manifest disease than natives.

Immunity.—One attack usually confers immunity, but this, like the artificial immunity conferred by inoculation, may occasionally be overcome by massive infection. In a series of 2,000 cases, fourteen persons were affected twice and one person three times (Osler, 1910).

Mortality.—Prior to 1910, the case fatality rate generally ranged from 10 to 20 per cent. In the last generation among cases of all ages carefully treated it has frequently declined to about 5 per cent. There is a tendency, however, to higher fatality rates in epidemics. The minimum mortality is found in the age group 5 to 10 years, and the maximum, under three years and over sixty years. The use of chloramphenicol in treatment seems likely to reduce the death rate materially.

Bacteriology.—(*S. typhi*, *E. typhosa* or *B. typhosus*) is a motile flagellated, gram-negative bacillus. It is resistant to freezing for months, and to a temperature of 60° C. for one hour : it has great powers of vitality in the moist state. It is killed in about five hours in sunlight and in dried earth, and consequently dust plays no great part in its dissemination. It is fairly resistant to coal-tar disinfectant solutions but is highly

susceptible to chlorination by minute amounts of hypochlorite in water supplies and swimming-baths. It can be cultured from the blood during the first two weeks of the disease, and often even in the third week.

Antigenic structure.—The bacillus has three known antigens, which are of great importance in epidemiology, diagnosis and treatment. The *H* or *flagellar* antigen is specific for this bacillus, and the corresponding H antibody when found in the blood serum denotes specific infection or inoculation with this organism. The *O antigen*, a deep somatic one, has two characteristics: (1) it is an indicator of endotoxin content of the bacillus, and (2) it is not entirely specific, but a group antigen related to the O antigen of other Salmonella organisms, *e.g. S. Enteriditis* (Gærtner.) The corresponding *O antibody* is an indicator of anti-endotoxin, and is typically present in high titre late in the acute stage (p. 1792). The *Vi antigen*, a superficial somatic one, is easily removed by repeated subculture of the organism. It is associated with the virulence and multiplication of strains. The corresponding *Vi antibody* is an expression of the body's resistance to the multiplication of the bacillus.

The Widal test for diagnosis has been made more precise by the differentiation of H and O antibody titres, now done as a routine (p. 1792).

Bacteriophage typing of Vi strains of *B. typhosus*.—This method of differentiation of virulent (Vi) strains of the organism was discovered by Craigie and Yen (1938) and has already proved of great value in tracing the sources and paths of infection during epidemics. Bacteriophage, isolated from the fæces of cases or carriers, usually lyses only the strain of the organism with which it was isolated. It can, however, be "conditioned" to any given Vi strain by growing it upon this strain for many generations, until it lyses this strain and no other. Thus, some twenty-two specific phages for known Vi strains have been built up. When a given strain is isolated from a case, discs of growth of the unknown organism on agar are spotted each with a different specific phage. After incubation for a few hours, the phage which is specific for the unknown strain produces a circular clear area of lysis in the centre of the disc of growth, while the other phages produce no effect. The phage type of the unknown strain is thus determined. The twenty-two odd phage types of *S. typhi* are indicated by group letters A to F and numbers, *e.g.* A, D4, E2, etc. The great majority of strains which have been isolated since this method was introduced are capable of being typed in this way, but about 16 per cent. have proved to be imperfect Vi forms or otherwise difficult to type. The method has been successful in providing clues to the source of infection in several epidemics, *e.g.* a milk-borne small epidemic in Bucks and Herts was traced after eighteen months to a carrier on a farm in Wilts over a hundred miles distant (Bradley, 1943). The differentiation of strains of *S. typhi*, unlike that of hæmolytic streptococci, is thus *not* done on a serological basis.

Symptomatology.—The symptoms of typhoid fever vary in children even more than in adults, from a mild ambulant febrile illness or an attack of diarrhœa to a severe prolonged and exhausting toxæmia. The in-

cubation period is usually about fourteen days but may be, in rare cases of massive infection, as short as three days; the upper limit of twenty-three days sometimes claimed may possibly include the early invasion period when symptoms are minimal. It is not uncommon for the infective material to contain mixed intestinal pathogens with consequent diarrhœa and vomiting within a few hours of the infection ("illness of infection") followed about a fortnight later by the onset of typhoid fever.

The onset is usually insidious with malaise, tired feeling, anorexia, headache and general pains and sometimes vomiting and abdominal discomfort. Not all of these symptoms may be complained of at first, and the patient may not feel ill enough to go to bed, but after three or four days he steadily becomes worse. Occasionally epistaxis takes place a few days after the onset. Rarely the onset is rapid, with chills or convulsions in children.

In a typical case during the first week, the temperature mounts gradually each evening eventually reaching 103° or 104° F. The pulse rate does not usually rise proportionately to the temperature, although in young children this sign is less constant than in adults. By the end of the week the pulse in the severer cases is of low tension and may be dicrotic. The tongue is coated except at the tip and edges which may be bright red. The back of the tongue tends to be dry. The abdomen shows some gaseous distension. There may be either constipation or diarrhœa, more commonly the former. The conjectivæ are clear. The mental condition tends to dullness and apathy, although this may be delayed to the second week, especially in children. There may be sleeplessness and mild mental confusion at night. A short dry cough is often troublesome and bronchitic sounds may be heard in the chest.

In the second week the fever remains high, with small morning remissions; the pulse becomes quicker; the expression is apathetic, and there is a malar hectic flush and moist skin. In a majority of cases, the characteristic eruption now appears in the form of scanty discrete small rose-red lenticular spots on the abdomen, flanks, chest and back. They vary in size from 1 to 3 mm. in diameter; they disappear on light pressure and re-appear when the finger is raised; they come out in successive crops during the second and third weeks. Occasionally they are so profuse as to invade the arms, legs and face; more commonly they are scanty, totalling less than half a dozen spots; sometimes they are absent altogether. They are metastases associated with the septicæmia, and typhoid bacilli can be grown from them. The spleen is now usually palpable to the extent of one or two fingerbreadths below the costal margin on deep inspiration. It is nearly always soft, and may be tender on pressure. Gastro-intestinal symptoms become more pronounced; the lips are dry; the tongue is dry and coated with a brown fur; sordes collect around the gums and teeth; diarrhœa is usual with watery yellow (pea-soup) stools, although in many cases constipation persists. Abdominal distension and discomfort is marked; some degree of deafness may be noted. In some cases respiratory symptoms with cough and dyspnœa are prominent, and there are signs of bronchitis, basal congestion or

pneumonia. In mild cases, on the other hand, defervescence may occur gradually or rapidly at the end of the second week.

During the third week, in the severer cases, the toxic state advances. Fever remains high, but with greater remissions. Exhaustion, prostration, emaciation, low tension pulse, low delirium and insomnia are prominent features. The extreme manifestation of toxæmia known as the " typhoid state " is characterized by dulled mental processes, apathetic aspect, " coma vigil "—the patient lying with open eyes but unconscious of his surroundings—tremor of tongue and lips, picking at the bedclothes, twitchings of the fingers and wrists, low muttering and peripheral circulatory failure. It is, however, rarely developed to this extent in children. These toxic symptoms are in some cases combined with a picture of urgent acute respiratory disease—generalized acute bronchitis, pneumonia or pleurisy. The two chief complications of the disease, intestinal hæmorrhage and perforation, occur at this time ; perforation is, however, rare in children.

During the fourth week the temperature as a rule gradually drops to normal, and all symptoms gradually subside. The toxic myocardial damage may, however, lead to sudden heart failure at this period. Sometimes a relapse (" intercurrent " type) sets in before the temperature has reached normal, and the fever, bacteræmia, rash and other symptoms appear all over again during the next two or three weeks. More commonly the fever ends in the fourth week, appetite returns and a slow convalescence sets in with subnormal temperature. This may be punctuated with the appearance of various complications, *e.g.* venous thrombosis in the limbs, subcutaneous or sub-periostal abscesses in ribs, spine, long bones, or toes, cholecystitis, neuritis and many others.

A *relapse* occurs in about 12 per cent. of cases, usually within ten days after subsidence of the primary attack. This illness is usually a little shorter than the primary fever. The above is a brief account of a moderately severe case of typhoid fever. There are, however, certain variations which occur in children.

Typhoid in the fœtus.—If a pregnant woman contracts typhoid fever the fœtus may or may not be infected. Abortion takes place in about 65 per cent. of the cases, usually in the second week of the disease. An infected fœtus dies *in utero* or shortly after birth. Typhoid bacilli have been cultivated from fœtal blood, presumably having passed through the placenta from the mother. The disease in the fœtus is a primary septicæmia with cachexia and without intestinal lesions.

Typhoid in infancy.—The clinical picture in infancy is variable. It frequently resembles that of entero-colitis with vomiting and diarrhœa as the prominent symptoms. The onset is often sudden with pyrexia of 102° F. or more, and may be accompanied by meningism, squint, drowsiness or stupor. The course tends to be relatively short—from a few days to two or three weeks. Dehydration is usually avoided by reasonable care.

Less frequently the picture is one of severe toxæmia, with sparse eruption of rose spots, enlarged spleen, diarrhœa, wasting, and sometimes

bronchitis or broncho-pneumonia, typhoid meningitis, or empyema and abscesses.

Perforation and intestinal hæmorrhage rarely occur in infants since there is little swelling or ulceration of lymphoid tissue. The intestinal wall may show only scattered areas of hyperæmia. Fatality is higher in these severe types up to 50 per cent. (Osler, 1910). Over-all fatality in seventy-five cases under two years of age was reported by Griffith (1912) as 16 per cent.

Typhoid in older children.—From five to ten years the disease tends to be mild and may even be ambulatory. Onset is usually insidious, but may be sudden with high fever, vomiting and meningism. Occasionally in children, the onset resembles a diffuse bronchitis, but the disease develops with high fever, wasting and severe general illness resembling tuberculosis. A positive blood culture or Widal reaction or defervescence setting in unexpectedly after eleven to fourteen days may point to the true diagnosis. The course is thus usually shorter than in adults; pyrexia generally lower; constipation is more common than diarrhœa; and abdominal tenderness more commonly suggests a diagnosis of appendicitis. The rash is frequently absent or scanty. Perforation and intestinal hæmorrhage are rare. Anatomically, ulceration of Peyer's patches and lymphoid follicles is superficial or does not occur at all. Complications are rare although relapses are more common than in adults. Case fatality at this age has seldom exceeded 5 per cent. After the age of eleven the disease tends towards the adult type. The typhoid state is, however, uncommon, listlessness and apathy taking its place, along with anorexia and wasting. Perforation and intestinal hæmorrhage, as in younger children, are uncommon.

Complications.—These are protean and can only be considered in outline.

Alimentary.—*Vomiting* is rare, except in infants, and at onset. *Meteorism* due to flatus in the atonic intestine is almost invariable. *Diarrhœa* is less frequent than constipation in children, but is a feature of the severer cases. If associated with curds in the stools, it may be the result of improper feeding and call for more dilute or citrated or peptonized milk mixtures.

Hæmorrhage may be of any degree from slight melæna or streaks of blood in the fæces to copious tarry or red blood passed per rectum. The latter is often associated with sudden collapse and symptoms of shock—pallor, cold sweat, anxiety, low tension rapid pulse and fall of temperature. Immediate transfusion may be necessary to save life, even at the risk of further hæmorrhage.

Perforation like hæmorrhage occurs most often in the third week as the sloughs separate from the Peyer's patches or solitary glands. There is sudden abdominal pain, but often no complaint if the patient is highly toxic. The temperature falls, the pulse rate rises and there may be a rigor or slight shivering. The rapid change in the patient's face indicates a serious turn; it becomes pinched, pale and anxious. Examination of the abdomen reveals at least one tender and rigid spot,

pressure on which makes even a listless apathetic patient wince. This, in such circumstances, is sufficient in itself to justify exploratory laparotomy. Absence of liver dulness is the next most valuable sign, provided that gaseous distension of the intestines is not too great. In a few hours, signs of general peritonitis appear, the temperature again rises, the pulse becomes more feeble, vomiting and hiccup may occur, and the visage shrinks into the typical Hippocratic facies. The chief difficulty in diagnosis arises from a pin-point perforation in which symptoms at first are minimal. Occasionally such perforations have been known to heal spontaneously, with subsequent abscess formation or adhesions. Perforation is almost invariably fatal unless operated on promptly. The prognosis in children is better than in adults. Out of twelve cases under six years old, six recovered after operation.

Cholecystitis is rare in children. It occurs usually in the third week and there is associated pain, tenderness and some rigidity in the right hypochondrium. Rarely the gall bladder perforates, giving rise to symptoms like those of intestinal perforation. A late result of cholecystitis is the chronic fæcal carrier condition and the formation of gallstone.

Appendicitis.—Like all fevers in children, typhoid fever may at onset present appendicitis-like symptoms. The writer has seen at least one case of almost every specific fever in which the abdomen has been opened for suspected appendicitis. Similarly, the symptoms may appear about the third week when the lymphoid tissue of the appendix swells, and then the differential diagnosis from perforation may be difficult but is usually capable of elucidation.

Parotitis.—This is usually due to oral sepsis and is consequently rare in children. Suppuration causes trismus and difficulty in feeding. All this should be prevented by a proper nursing toilet of the mouth, and by chemotherapy at the first sign of onset.

Pancreatitis, *hepatitis* and *splenic abscess* are rare.

Genito-urinary.—Mild albuminuria of toxic origin is frequent. In the rare form known as " nephro-typhoid " the illness commences with symptoms of acute nephritis. *Retention of urine* is common, especially during the most toxic phase in the third week. *Typhoid bacilluria* is rare in the first but common in the second week of the disease. It then disappears, but may reappear as the chronic or intermittent *urinary carrier* condition. This may or may not be associated with small renal abscesses, pyelitis or cystitis, or even with lithiasis. A pyelogram of the urinary tract should be used in the investigation of chronic urinary carriers.

Respiratory.—Pneumonia-like symptoms at *onset* occur in some cases. *Laryngitis* and *small discrete ulcers of fauces and pharynx* are rare in children. Some degree of *bronchitis* is almost invariable in typhoid fever. Sometimes this passes on to broncho-pneumonia and respiratory symptoms dominate the clinical picture. In such cases, sulphonamides, penicillin or appropriate antibiotic must be given without delay, for the pneumonia is often due to secondary pyogenic organisms. *B. typhosus empyema* occasionally occurs after broncho-pneumonia or in convalescence.

Circulatory.—*Toxic myocarditis* is a dominant feature of all severe cases not treated with chloromycetin from the third week onwards, and calls for supreme nursing care to avoid heart failure. Care in convalescence must be prolonged so as to give time for the heart's recovery. The signs in typhoid are similar to those in any severe fever. *Pericarditis* may occur, especially in infancy in association with pneumonia. *Endocarditis* is rare. *Arteritis* of limb vessels has been followed by gangrene, and of cerebral vessels by hemiplegia, aphasia or death. It is rare but may occur in children. *Venous thrombosis* is more frequent, especially in children over ten years. The small veins of the calf of the leg usually become first thrombosed, leading to femoral thrombosis and œdema of the limb.

Nervous.—*Meningism* at onset is common, in infancy especially. True typhoid *meningitis* with *S. typhi* in the spinal fluid is, however, very uncommon. *Delirium, convulsions, stupor* are part of the toxic phase of the disease. *Psychoneurosis* and *pyschosis* of convalescence are rare in children.

Peripheral neuritis may occur during the fever or in convalescence. There is pain or numbness with or without loss of sensation and motor power in arms and legs.

Tender toes, hyperæsthesia of the toes, so that the weight of the bedclothes cannot be borne, may be due to a local peripheral neuritis or to a periostitis.

Encephalitis sometimes followed by Parkinsonism has been described (Huber, 1937).

Bones, joints, muscles.—*Periostitis* with silent, slowly forming bone abscesses, *e.g.* in ribs, tibiæ, frontal bones or vertebræ may occur in convalescence and develop slowly for months or years before breaking down and discharging pus. The pus contains *S. typhi* in pure culture. "Typhoid spine," which results in absorption of an intervertebral disc and erosion of adjacent vertebræ, is rare under fifteen years. The painful spasm induced in the neighbouring muscles may suggest a diagnosis of lumbago or "rheumatism." It is readily cured by rest for a few months in a plaster cast, thus responding to treatment much more readily than tuberculous caries of the spine.

Zenker's degeneration of muscles, especially the rectus abdominis, or pectoralis major, may lead to hæmorrhage or rupture. Suppuration may occur and *S. typhi* is then found in the pus.

Bedsores.—In any prolonged fever, especially with incontinence, a patient is liable to bedsores, from pressure necrosis, but these should be avoided by good nursing technique.

Alopecia.—Complete loss of hair is a sequel which may occur after prolonged fever. The hair returns after a few weeks or months.

Ears.—Temporary *deafness* is not uncommon in the acute stage. *Otitis media* is due to secondary hæmolytic streptococcal infection.

Eyes.—*Conjunctivitis, keratitis, iritis, retinal hæmorrhages, optic neuritis,* or *strabismus* are all rare accompaniments of the toxic process.

Diagnosis.—In any continued fever of four or five days' duration

without definite localizing signs, diagnostic tests for typhoid fever are usually indicated. Clinically suspicious early signs are a slow pulse rate in relation to the temperature, epistaxis, a dry tongue, and some abdominal distension or diarrhœa. *Blood culture* is the most reliable laboratory test during the first week, and with the newer culture media, it is usually positive in the second and often also in the third week.

A heat sterilized all-glass syringe and needle should preferably be used and the skin in front of the elbow cleansed with ether followed by iodine and then by alcohol if necessary to show up the vein. About 6 c.cm. of blood should be withdrawn from the vein, great care being taken not to touch the shaft of the needle with the fingers. Some 3 c.cm. of blood is injected into a bottle of bile salt broth (for the enteric group of organisms) and 3 c.cm. into a bottle of glucose broth (for pyogenic organisms). If no culture media are available at the bedside, the clot may be sent to the laboratory in a sterile bottle for "clot culture." This is often successful in typhoid. The blood clot is picked up with sterile forceps in the laboratory and dropped into bile salt broth. Blood culture should always be performed, if possible, when the patient's temperature is high, preferably over 101° F.

Culture of fæces or of a rectal swab by the newer methods is also usually positive in the first week, but constipation frequently limits this method. *Culture of urine* is somewhat uncertain, owing to intermittent excretion. The Vi agglutination test is positive from the first to the fifth day, after which it disappears in some 25 per cent. of cases (Boyd, 1939). A blood count shows leucopenia with relative lymphocytosis, and often also thrombocytopenia.

During the second week, particularly from the tenth day, the Widal reaction becomes positive. Titres should be at least 1 in 30 for H and 1 in 50 for O agglutinins in an uninoculated subject. In an inoculated subject the Widal reaction is unsatisfactory since any fever may give rise to an anamnestic reaction with H agglutinins. A rising O titre would, however, be suggestive, as high O antibody indicates well-resisted infection (p. 1786). When a patient is first seen in the second week, both blood culture and Widal test should be performed. They are usually both positive. Fæces and urine culture may be confirmatory. The important clinical signs in the second week are the eruption of rose spots, splenic enlargement (both of which, however, may be absent), abdominal distension, dry tongue, relatively slow low-tension pulse and increasing toxæmia.

Differential diagnosis.—In infants and young children typhoid and paratyphoid fevers, especially in the earliest stage, frequently present a clinical picture of *gastro-enteritis*, and sometimes of *broncho-pneumonia* or *meningitis*. The following diseases in the first few days may present *continued fever* liable to be mistaken for typhoid : *typhus fever*, *septicæmia*, *cystitis and pyelitis*, *undulant fever*, *rheumatic fever*, *malignant endocarditis*, upper respiratory *hæmolytic streptococcal infections* (especially *sinusitis*), *glandular fever*, *acute miliary tuberculosis*, *influenza*, *pneumonia*, *infective hepatitis*, *psittacosis*, *tularæmia* and *chronic malaria*.

Other diseases with prominent *gastro-intestinal symptoms* which may be mistaken for typhoid include : "food poisoning" (vomiting and dehydration more prominent), "gastric influenza" or virus diarrhœa, appendicitis and other forms of "acute abdomen." The differential

diagnosis in typhoid fever often requires considerable clinical experience, the application of many clinical tests and the full resources of a well-equipped laboratory.

Pathology.—The specific lesion is the lymphoid hyperplasia of Peyer's patches, solitary glands in the colon (affected in about one-third of the cases), mesenteric glands and spleen. About the third week, the swollen lymphoid tissue sloughs, producing oval ulcers in the long axis of the gut, which may be associated with perforation of the serous coat and hæmorrhage. In infants and young children lymphoid lesions are inconspicuous or absent; there is generalized ileo-colitis with scattered hyperæmic areas. The organs generally show the toxic changes associated with a severe toxæmia and septicæmia. These have been noted under "complications." Special features are the enlarged catarrhal gall bladder, and occasionally miliary abscesses in the kidneys.

Blood picture.—Throughout the acute stage there is a *leucopenia* generally of 4,000 to 5,000 cells per c.mm. with relative lymphocytosis. There is also an *eosinopenia* and a *thrombocytopenia*. In convalescence a post-infective lymphocytosis and sometimes an eosinophilia are usually found. When the complications pneumonia, severe hæmorrhage or suppuration arise, a blood count shows a polymorphonuclear leucocytosis. The red cells and hæmoglobin always show some degree of secondary anæmia.

Prognosis (see "mortality," p. 1785). Except in severe cases in infants, the prognosis is better in children than in adults.

Treatment—may be considered under the following heads: (1) Nursing, (2) Dietetic, (3) Specific, (4) Symptomatic, (5) Surgical.

(1) Nursing.—In no disease are good nurses more important. Their chief tasks are: (*a*) to maintain a clean mouth by two-hourly swabbing, if necessary, of tongue, gums and teeth with a bland antiseptic solution, *e.g.* glycothymoline followed by inunction of the lips with boro-vaseline; (*b*) to maintain an intact skin, free from bedsores by daily washing with soap and water, daily back rub with spirit and powder, protection of pressure points, *e.g.* heels, frequent turning of the patient, and use of a water bed or air-ring or, preferably, of a "Sorbo" rubber mattress; (*c*) to encourage the patient to take adequate fluids and as much first-class protein diet as possible in spite of anorexia; (*d*) to reduce temperature and toxæmia by tepid sponging when the temperature is over 102° F.; (*e*) to conserve the patient's strength and keep him comfortable and as cheerful as possible; (*f*) to prevent the spread of infection by prompt disinfection of all discharges and of soiled bed linen, clothing and gowns, and by personal cleanliness including hand washing before leaving the patient and before food. Stools should be mixed with twice their volume of 1 in 10 "white disinfectant" solution and allowed to stand four hours before being poured into the sluice. The bedpan should be sterilized by boiling or steeped in disinfectant for several hours after cleansing. The urine should be mixed with an equal volume of 1 in 10 "white disinfectant" solution and dealt with likewise. All attendants on a case of typhoid

fever should be inoculated with T.A.B. vaccine at once if that has not previously been done. There should be no hesitation to do this from fear of a supposed "negative phase," for there is no sound evidence in support of such an idea. Food should never be consumed by staff in ward kitchens.

(2) DIETETIC.—Much that is dangerous or impracticable has been written on the dietetic treatment of typhoid. The principles are simple: (*a*) maintain adequate fluids; (*b*) maintain adequate calories, first-class protein and vitamins to prevent wasting and under-nutrition; (*c*) avoid rough indigestible material, *e.g.* coarse vegetable fibres; and (*d*) make a daily examination of the patient's abdomen, and daily inspection of his stools before ordering or changing a diet and modify the diet if there is diarrhœa or undigested food in the stools. Milk, eggs, steamed white fish, minced meats, jellies, corn flour, Benger's food, cream, chocolate, mashed carrot and potato, fruit juices, clear broths and tea can all be used in the acute stage according to the degree of toxæmia and the skill and perseverance of the nurse. It is a mistake to half-starve a patient ill with this disease. The better the patient's nutrition is maintained the more easily does he overcome his toxæmia. Even after hæmorrhage or laparotomy for perforation it is essential to persuade the patient to eat well. Timid dieting by inexperienced doctors and nurses is one of the commonest and worst errors in the management of this disease. The limitations imposed by the patient's anorexia are sufficient to prevent over-feeding. It is impossible to give a diet of 4,000 calories daily throughout the fever to an adult, or the corresponding amount to a child, as is sometimes advocated. The maximum daily amount for an adult is 2,500 calories, and for a child correspondingly according to age and weight. The important thing is that the diet should be as generous as possible and contain a high proportion of first-class protein.

For an infant, the importance of adequate nutrition is also paramount. Milk feeds, however, may require special adjustment, *e.g.* citration or peptonizing or suitable grading of the strength of mixtures, in the event of intolerance or the appearance of curds in the stools.

(3) SPECIFIC. (*a*) *Therapeutic serum.*—The best therapeutic serum so far produced for typhoid fever was introduced by Felix (1935). The new principle in this serum is its rich content in O and Vi antibodies. It is, however, a variable product with little action except early in the disease, *e.g.* the first week. It has now been superseded by chloramphenicol.

(*b*) *Sulphonamides.*—These drugs have proved valueless in the ordinary form of typhoid fever. But in cases in which acute respiratory disease shows signs of developing, it is important to employ sulphonamides or penicillin immediately without waiting for the established signs of pneumonia. This principle is of special application in children. Chloramphenicol is, however, generally effective in the pneumonia of typhoid, and is to be preferred.

(*c*) *Penicillin-sulphathiazole.*—Bigger (1946) showed experimentally in animals that there was a synergistic action of these two drugs on

B. typhosus infections. Practical experience with this combination has been disappointing and it is now superseded by chloramphenicol.

(*d*) *Specific bacteriophage.* –Intravenous bacteriophage generally produces violent reactions—rigors, hyperpyrexia, etc., highly disturbing to the patient and must be considered unsatisfactory and dangerous, even in the treatment of chronic carriers.

(*e*) *Antibiotics. Chloramphenicol* (chloromycetin) is by far the best. It has revolutionized the treatment of the typhoid-paratyphoid fevers and greatly reduced mortality and complications. It appears to act at any stage of the acute disease, producing a notable amelioration of symptoms after a lag period of forty-eight hours. The temperature usually falls to normal in two to five days. Local inflammation or ulceration in the intestine and other organs often persists, however, for some days after the temperature is normal and toxæmia overcome. Diarrhœa may persist and even perforation and hæmorrhage may occur in an afebrile patient. During the course of treatment *S. typhi* disappears from blood, stools, and urine, but its growth is merely inhibited, and it may reappear and cause a relapse up to about thirty days, after withdrawal of the drug. Relapses, however, respond to the drug as rapidly as does the primary attack. Occasionally during the first forty-eight hours of treatment rigor, collapse or delirium may occur. This has been interpreted as a sort of Herxheimer reaction. The drug is given by mouth in capsules of 250 mgm. in a daily dose of 50 to 100 mgm. per kilo. body weight in divided six-hourly doses for a period of five to ten days. *Aureomycin* has not proved to be so effective in this disease.

(4) Symptomatic.—For *constipation.* Leave untreated for as long as fourteen days or more except when the abdomen is distended and the patient uncomfortable; in that case a soap and water or plain water enema may be given not more often than every third day; for *diarrhœa* with small frequent irritating stools, a starch and opium enema (3 to 15 minims of tincture of opium according to age in 2 oz. starch mucilage) is often effective: for *insomnia* chloral or a suitable dose of a barbiturate, *e.g.* somnifaine: for *hæmorrhage* a suitably graded dose of morphine according to age and plasma and blood transfusion if severe: for *tympanites*, an icebag suspended from a bed cradle. Whey may be substituted for milk: for *toxæmia* with threatened dehydration, dextrose-saline by continuous intravenous or rectal drip.

(5) Surgical.—In every case of suspected perforation, immediate laparotomy is indicated. The site of the perforation is often found just below the spot of maximum tenderness indicated by a co-operative patient. The ileum should first be examined, commencing at the ileo-cæcal valve. If no perforation is found the colon must be explored from the cæcum onwards. Perforations in the ascending and transverse colon are not rare, especially in paratyphoid fever. Occasionally the gall-bladder perforates. Multiple perforations, or one occurring shortly after the other, should be borne in mind. At least two desperately ill cases have been reported with perforation diagnosed clinically and treated with chloramphenicol, streptomycin and penicillin, and subsequent recovery without operation.

Carriers.—The chronic carrier condition following the disease is much less common in children than in adults. Nevertheless it occurs even as early as three months old. One baby of this age infected nine other persons. Quite a number of children of school age are known to be carriers. Before discharge from hospital every case should have three successive negative reports on fæces and urine, and, in addition, the blood should be examined for Vi agglutinins both at the time of discharge and, if present, three months later. The prophylaxis of the disease in this country in future demands the registration and control of as many carriers as can be found, since most outbreaks originate from unknown carriers.

Urinary carriers are usually freed from their organisms by sulphonamides or chloramphenicol given for a few days. Relapses, however, may occur. The intermittent urinary carrier must be kept under observation and examined from time to time, the examination including a pyelogram. Fæcal carriers should have the duodenal juice investigated for *B. typhosus*. If the organism is present, consideration should be given to cholecystectomy. This operation fails, however, in at least 25 per cent. of cases, and it is doubtful whether it is justified in a child. Penicillin-sulphathiazole, in doses of 500,000 units penicillin and $7\frac{1}{2}$ grammes sulphathiazole daily for eight days, has been successful in a few chronic carriers and has failed in most. Chloramphenicol also fails in carriers. The chronic fæcal carrier is still an unsolved problem.

Vaccine prophylaxis.—The vaccine used for prophylaxis against typhoid and paratyphoid fevers in Europe contains 1,000 millions of *B. typhosus* and 750 millions each of *B. paratyphosus A* and *B.* For use in certain areas of the world 750 millions of *B. paratyphosus C* is added. The vaccine must be rich in Vi and O antibodies. The superiority of the British Army vaccine, in which Vi strains are used, over that used in the Italian Army, was shown by Boyd (1943). The very low incidence of typhoid in the last and previous wars, in spite of great opportunities for infection, is usually held to have demonstrated the protective value of T.A.B. inoculation. Felix (1941) showed that Vi antigen was reduced by heat-killing of vaccines but not affected when the vaccine was killed by 75 per cent. alcohol, preserved in 25 per cent. alcohol and stored at a temperature of 4° to 10° C. This alcoholized vaccine was for a time generally adopted but heat-killed vaccines are again in use. Reactions are lighter in alcoholized than in heat-killed vaccines, and the dosage is less. For women and older children two doses are given at two weeks interval, 0·2 c.cm. and 0·4 c.cm. respectively; for younger children *pro rata*. Every person who is liable to special exposure to typhoid infection should be inoculated and then re-inoculated annually.

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PARATYPHOID FEVER

Another disease, closely resembling typhoid fever, only much milder in its manifestations, is caused by one of the paratyphoid group of organisms. In this country paratyphoid B is quite as common in children as ordinary typhoid fever. Paratyphoid A is practically unknown, whilst

Fig. 581.—An Unusually Widespread Rash in a Case of Paratyphoid B. Fever.

a paratyphoid C infection has occasionally been found in chronic bone abscesses, presumably following a mild form of generalized infection from this organism. The disease is more often *food-borne* than water-borne. Cream fillings of pastry have given rise to several epidemics.

Symptomatology.—The onset is similar to that of typhoid fever, but the symptoms are generally less severe. The illness begins with anorexia, headache and irregular fever, which, in the absence of classical signs of diarrhœa, splenomegaly and a rash, are apt to be puzzling. Many cases of paratyphoid in children are therefore diagnosed by a process of exclusion, when after all other investigations have given no indication, a Widal test proves positive. The abdomen is usually distended, the tongue is moist and coated and, except in infants, constipation is the rule. Labial herpes is common and bronchitis frequently present. The temperature is not as high, is of remittent rather than continued type, is less

prolonged than in typhoid fever, and may fall in two or three weeks by quick lysis. The rash tends to be more profuse than in typhoid and the rose spots rather larger—up to 4 mm. in diameter. Relapses occur, but complications are uncommon and recovery generally takes place.

Diagnosis.—This depends on blood, fæces or urine culture, or on the agglutination reaction of the patient's serum after the tenth day of the disease. In testing the patient's blood in a suspected case, agglutination reactions are done as a routine against *B. typhosus*, *B. paratyphosus A*, and *B. paratyphosus B* and sometimes *Br. abortus*.

Pathology.—Typical ulceration of Peyer's patches may not be found, but a superficial ragged ulceration has been noted in the ileum, just above the ileo-cæcal valve, and in the colon.

The **prognosis** is good. About 4 per cent. of the recorded cases have proved fatal, but this should be reduced with chloramphenicol treatment.

The **treatment**, prophylaxis and nursing precautions are exactly as for typhoid fever. Chloramphenicol, however, often acts more slowly in paratyphoid B than in typhoid fever.

INFLUENZA

The name influenza derives from "influentia cœli" or the cosmic influence to which the epidemics of the Middle Ages were attributed.

Epidemiology.— The disease is acute, highly infectious and characterized by general febrile disturbance, respiratory inflammation of variable degree and occasionally by gastro-intestinal or nervous symptoms and nervous sequelæ. Serological studies suggest that it has a wide endemic existence in the form of a mass of inapparent or sub-clinical infection punctuated by sporadic cases or small outbreaks. In Europe, the United States of America and to some extent in the Southern Hemisphere it tends to assume epidemic proportions every second or fourth year, generally in the first quarter of the year in the Northern Hemisphere. This incidence is, however, subject to considerable variation and cannot as yet be predicted. Owing to its short incubation period, its high infectivity and the short duration of the immunity produced, it spreads rapidly and widely along lines of communication. Thus, an epidemic may cover a whole country within a few weeks.

At intervals of thirty to sixty years since the year 1500 it flared up into virulent pandemics which spread over Europe and often round the world in the course of a few months. The greatest was that of 1918-19, which was estimated to produce 525 million cases with 21 million deaths. Everywhere mortality was heaviest in young adults—a characteristic of a "new disease" or a new infective strain (Burnet, 1940). It occurred in three waves. The first of these was virulent enough to spread during the summer. The second, starting during the autumn, was the most virulent of all. It produced a fatal form of interstitial broncho-pneumonia, and attacked young persons as well as old. The third wave, in 1919, was less virulent but caused numerous deaths, especially in older persons.

The cause of such sudden changes in virulence is unknown, but may be related to gene mutations of the virus. In tobacco mosaic disease the gain of a few thousand atoms by the virus molecule is known to transform it into a variety that produces the much more virulent disease "acuba" (Fenton, 1945); Shope (1943) has shown that swine influenza may be endemic in many countries awaiting suitable conditions to start an epidemic. Andrewes (1943) in an attempt to explain the vagaries of endemic, sporadic, epidemic and pandemic influenza postulated seven grades of influenza virus of ascending virulence. The first, he thought, would be a harmless latent saprophyte in human cells; the second would be the unknown viruses which give rise to the mild influenza provisionally designated Y, since therein A and B virus antigens and antibodies are not demonstrable; the intermediate ones would be A and B viruses of various grades; and so on to the seventh grade, that of autumn 1918, the most deadly ever known.

In addition to the easily recognizable pandemics, it seems probable that there are others only recognizable as such by the use of laboratory methods simultaneously in various parts of the world. Thus there is evidence that influenza B virus had a world-wide distribution associated with many localized and mild outbreaks in 1945–46 (Dudgeon *et al.*, 1946).

The epidemiology of influenza has always been obscured by the existence of many other virus infections of the respiratory tract which produce a similar and sometimes indistinguishable clinical picture. They include the common cold, non-hæmolytic-streptococcal pharyngitis, "grippe" or febrile respiratory catarrh and virus and rickettsial pneumonias. Amongst all those conditions, influenzal and non-influenzal, there is much overlapping of clinical symptoms and signs, and even in the setting of an influenza epidemic confusion with non-influenzal disease is common. This uncertainty will remain until these various infections can be sorted out by laboratory tests. At present only influenza A and B, some virus pneumonias, *e.g.* psittacosis, some rickettsial pneumonias, *e.g.* Q fever, and to a limited extent primary atypical pneumonia can be so distinguished and the tests are still the function of a virus reference laboratory.

Bacteriology.—*Hæmophilus influenzæ*, discovered by Pfeiffer in 1892, was long suspected to be a secondary invader, since it could be isolated from the respiratory tract in health as well as in many kinds of disease. Not until 1933 was the virus ætiology of influenza proved, when Smith, Andrewes and Laidlaw in London succeeded in infecting ferrets from the filtered throat-washings of influenza patients. This agent has since been given the designation *influenza A virus*. It has been isolated in many outbreaks of varying severity in Britain, U.S.A. and Australia. Studies in these countries have shown that there is a considerable group of A viruses, exhibiting minor antigenic differences amongst themselves but having the common property of inducing the formation of A antibody in the blood serum of those infected. In 1940, Francis and Magill, working independently in America, isolated influenza B virus, so called because it has no serological relationship with virus A. The B virus also consists of a group of closely related strains all of which give rise to B antibody, but not to A antibody. Most epidemics are due mainly to A or mainly to B virus, but in any given epidemic there is usually a certain admixture.

In the American and West Indian outbreaks of 1940 and 1941, not only

were A and B types both found, but there were certain cases from which viruses were not recovered and which exhibited no antibody to either A or B. Hence the provisional designation of influenza Y for such unclassified groups of cases, which appear on clinical and epidemiological grounds to be due to influenza virus, but in which no recognized virus or antibody can be demonstrated.

The available information suggests that virus A is commonly associated with the more virulent and widespread epidemics and with mortality from pneumonia, while virus B is more associated with insidious onset, mildness, sporadic incidence and a tendency to attack younger age groups (Dudgeon *et al.*, 1946). But such clinical distinctions are by no means certain. Virus A can be sporadic and mild and virus B epidemic and explosive.

Cultivation of the virus.—This has been greatly simplified by the method of inoculation of filtered throat-washings into chick embryos (Burnet, 1935; Hirst, 1945). The amniotic fluid drawn off after three or four days' incubation provides a suspension of the virus. A simplified technique is the use of non-filtered material along with soluble streptomycin and penicillin for injection into the eggs.

Morphology.—Studies with the electron microscope have shown particles presumably representing virus A as bean-shaped or kidney-shaped bodies about 80 mμ across. Virus B looks much the same but is significantly larger, being about 100 mμ across (Sharp *et al.*, 1943).

Immunity.—In testing for antibody in blood serum, virus neutralization and complement fixation methods were first employed. These methods were somewhat cumbrous. A great advance was made by Hirst (1942) when he discovered that influenza virus agglutinated chicken erythrocytes. When serum containing antibody was added to the virus suspension before the agglutination test it was found that agglutination of the erythrocytes was inhibited. This "agglutination-inhibition" test has now become the standard test for antibody. With the use of this relatively simple method detailed studies in America have shown: (1) Except in persons possessing an initially high antibody titre, a rise of serum antibody occurs with an attack of influenza, and commonly also during an epidemic in persons without apparent clinical infection. Thus it has been estimated that, during the American epidemic of 1943–44, the subclinical infections were at least twice as numerous as the clinical cases (Hirst *et al.*, 1944); (2) both in experimentally induced and naturally occurring influenza there is a zone of serum antibody concentration above which protection against clinical influenza is reasonably assured; (3) the duration of solid immunity following the natural disease is short—probably only a few months. Repeated A infections have been observed in the same person within a period of two years.

Symptomatology.—The incubation period is short, in virus A infections as short as twenty-four to forty-eight hours. The symptoms of influenza are variable and cannot be precisely differentiated from those of other virus infections of the respiratory tract. Different grades of influenza virus reacting with different degrees of resistance produce clinical illness

varying from simple coryza to fatal broncho-pneumonia. The later stages of influenzal and non-influenzal virus respiratory disease, when complicated by secondary bacterial infection, may be similar. It may be said generally, however, that in influenza, constitutional symptoms are prominent at onset with respiratory symptoms developing later, whereas in non-influenzal virus infections, respiratory symptoms tend to be prominent from the start. Further, influenza appears to be more particularly associated with gastro-intestinal and nervous symptoms and with nervous sequelæ. In infants and children influenza is not usually as severe as in adults. Fever and respiratory symptoms usually subside in a few days, but the child is weak and anæmic afterwards ; there is always the danger, however, of broncho-pneumonia.

Constitutional symptoms are constant, usually short (three to five days) and may be the only manifestation (febrile type). Onset is usually rapid with fever, chills, headache and general pains, sweating, dizziness, anorexia and a varying degree of prostration. Commonly this is followed within a day or two by substernal discomfort and short dry cough. This may gradually subside along with the febrile disturbance or may extend to any degree of respiratory tract involvement.

Respiratory symptoms commonly accompany the systemic ones. They usually follow but occasionally precede them. Symptoms vary from those of a mild naso-pharyngitis, laryngitis or tracheitis to those of a fatal broncho-pneumonia. They include : rhinorrhœa, nasal obstruction, sore throat (naso-pharyngitis), swellings of eyelids and cheek (sinusitis), croupy cough, hoarseness, loss of voice, stridulous breathing (laryngitis), sub-sternal pain with short cough (tracheitis), expectoration (bronchitis), dyspnœa, cyanosis (broncho-pneumonia), heliotrope cyanosis (interstitial pneumonia), pain in side (pleurisy and empyema). Symptoms relative to extensions of the respiratory tract include : conjunctival injection or discharge, photophobia (conjunctivitis and dacryocystitis), earache with blood blisters on the tympanic membrane, otorrhœa, mastoid tenderness or swelling (otitis media and mastoiditis), pain and swelling in the neck (adenitis). During an epidemic the majority of cases follow a reasonably consistent course.

When broncho-pneumonia occurs in the milder outbreaks, it seems to be usually associated with secondary bacterial infection with such organisms as hæmolytic streptococci, pneumococci, or *H. influenzæ*. In the most severe influenza epidemics pneumonia follows so closely after onset that the highly virulent virus itself may be responsible. In the worst cases an interstitial broncho-pneumonia or pneumonitis occurs and may be accompanied by heliotrope cyanosis of mucous membranes and skin—a highly fatal condition. Physical signs are those of patchy collapse and capillary bronchitis, but not of massive consolidation, that is, percussion only slightly impaired, diminished air entry and fine râles. Histologically there is gross round-cell infiltration with œdema and hæmorrhages of the interstitial supporting tissue around bronchioles and alveoli. There is no massive consolidation in the alveoli themselves. In recent epidemics, however, synchronous influenza and pneumonia has been

found to be associated with secondary *staphylococcus aureus* infection in some cases. This is a serious combination often responding badly to penicillin therapy.

Nervous symptoms are especially prominent in some cases. These patients have usually an abrupt onset with high fever, vomiting, headache, pain behind the eyes and sometimes convulsions. Dizziness, restlessness and insomnia are common. Neck rigidity and head retraction (meningismus) may simulate meningitis, especially if accompanied by delirium or stupor. Myelitis with resulting spastic paraplegia may suddenly appear. In children this usually clears up after some weeks or months, the prognosis being much better than in adults. A clinical syndrome suggesting encephalomyelitis has been recorded, but whether of poliodastic or myelinoclastic type is not clear.

Gastro-intestinal symptoms.—Anorexia, vomiting, abdominal pain and watery diarrhœa are common in children, especially in infants, at onset. If they continue, dehydration, with prostration and collapse is the danger. In some epidemics of influenza cases occur in which these are the presenting symptoms, and which also remain predominent throughout the illness. Virus diarrhœa is now thought to be an infection quite distinct from influenza, but extended serological studies for influenza antibody in diarrhœal cases are much needed in order to clarify this subject.

Complications are commonly associated with secondary bacterial infection. The virus phase in the respiratory tract often merges imperceptibly into the secondary bacterial phase. Since respiratory symptoms and complications are thus often indistinguishable, they have been grouped together above. *Myocarditis* should be looked for. An indication of it is occasionally obtained when an over-normal systolic blood pressure, *e.g.* 160 mm. Hg, drops during the course of the illness to an under-normal one, *e.g.* 105, with a low pulse pressure. In children myocarditis is less important than in adults, but it may be found to be part of the general picture of prostration, debility and depression during and after influenza. This has a bearing on the treatment. *Pericarditis*, *endocarditis*, *phlebitis*, *arthritis* and *nephritis* are rare events. Relapses are not uncommon.

Blood picture.—Leucopenia in the virus phase and polymorphonuclear leucocytosis in the secondary bacterial phase are so interwoven that no characteristic blood picture of the disease can be described. Hughes (1938) during an influenza A outbreak found the average leucocyte count in the early stages of uncomplicated cases to be 7,000, with limits of 4,000 and 14,000. Secondary anæmia is usual in children.

Diagnosis.—During an epidemic there is usually little difficulty in diagnosis, but the influenza-like stage of other infections is apt then to be confused with "flu." Serological tests for rising antibody titres are diagnostic in A and B virus infections. A pair of blood samples are examined, one at onset and the other ten days later. Cultivation of the virus from the naso-pharynx during the first week of the disease by the chick embryo technique is simpler than by ferret infection, but it

fails with certain strains. None of these laboratory procedures is yet in routine use.

Differential diagnosis. "*Febrile catarrh.*" The main points in differential diagnosis are that cases of influenza tend to have a sudden onset without preceding catarrhal symptoms, and with constitutional symptoms such as headache, malaise and muscular pains usually prominent; in the "febrile catarrh" type of infection, the onset is more gradual, coryza, cough and sore throat tend to predominate and constitutional symptoms are less evident. This distinction does not always hold with the milder clinical cases of influenza in which, also, secondary bacterial infection is more common than in the severer cases. "*Primary atypical pneumonia*" is a virus disease with relatively few physical signs, with well-marked X-ray pulmonary infiltrations, with absence of leucocytosis and of response to sulphonamide or penicillin treatment, and a proportion of cases give a positive "cold agglutinin" test or may yield agglutinins with streptococcus MG. from the second to fifth week of the disease (Thomas, *et al.*, 1943). The prodromal stages of fevers, *e.g.* measles, smallpox, typhoid, typhus and glandular fevers, may be confused with influenza. The same applies to the stage preceding localizing signs in such infections as septicæmia, poliomyelitis, acute lobar pneumonia, tuberculosis, psittacosis, or malignant endocarditis. Much clinical experience and many laboratory tests may be required to exclude such conditions.

Period of infectivity.—This may last for a week, but is usually not more than three or four days.

Prognosis is usually good in children, except in severe epidemics in which broncho-pneumonia is common. Bronchiectasis is always a possible sequela whenever broncho-pneumonia persists for more than two weeks. In infants, gastro-enteritis with dehydration is grave. Older children and young adults tend, however, to recover rapidly and show no tendency to develop a post-influenzal state such as may threaten the more elderly.

Treatment.—*Isolation* is desirable, especially in coughing and sneezing patients. *Diet* should be as nourishing as the appetite will allow. A critical attitude is justified towards many of the remedies in common use. *Diaphoretics*, *e.g.* aspirin and hot drinks are comforting in the "dry" stage of respiratory inflammation but should not be overdone when sweating is already present. *Purgatives and diuretics* are usually unnecessary and may be harmful. *Alkaline drinks* may be pleasant but are not usually necessary to combat the mild acidosis of the early acute stage. *Counter-irritants* in the form of poultices or plasters are comforting and have a psychological value. A hot-water bottle or electric heating pad are simpler means of providing the same comfort. *Cough mixtures* are inheritances of folk-lore. Expectorants in the usual dosage do not change the volume or viscosity of the sputum. In large doses they are slightly emetic, tend to increase the flow of saliva but not of exudates, and disturb digestion (Alstead, 1939). *Local therapy, e.g.* gargles, sprays and paints, tend to disturb the coating of mucus and ciliary activity which are part of the natural defence mechanism. Inhalations of menthol medicated

vapour are soothing in the dry congestive stage. *Potassium chlorate*, 5 grains to the ounce, lightly gargled and swallowed seems to aid resolution of the inflammatory process. *Oily sprays and nose drops*, if long continued, may lead to lipoid pneumonia. *Nasal vaso-constrictors, e.g.* ephedrine and amphetamine, have their place in extreme nasal congestion and acute sinusitis to promote drainage. They should be used moderately since otherwise they lower the protective effect of the local inflammation, lead to secondary congestion and prolong acute rhinitis.

Rational therapy includes rest in bed and warmth to promote rapid recovery and prevent complications ; isolation from the healthy to prevent secondary cases ; nursing care of the mouth, nares, skin, and bowels when necessary, especially when the illness is prolonged ; tepid sponging for high temperature ; analgesics and sedatives for pain and sleeplessness, *e.g.* codeine, Dover's powder, barbiturates and salicylate compounds ; dextrose saline by mouth, rectally or parenterally by drip, for severe vomiting and dehydration ; adjustment of the diet for diarrhœa ; local volatilized menthol or amphetamine inhalations or ephedrine drops in strict moderation to control nasal obstruction and so promote sleep ; gentle local irrigation or spraying of the nasal cavity with iso-tonic and iso-*p*H solutions (*p*H 6·8),[1] if necessary when muco-purulent secretion is purulent and thick ; blowing of the nose as seldom as possible, and then gently through both nostrils at once, preferably into disposable paper handkerchiefs or rags ; oxygen with 5 per cent. CO_2 may be tried as an expectorant in the later subacute stage when there is profuse bronchial secretion ; codeine phosphate $\frac{1}{8}$ grain or less according to age to quiet over-active cough reflex.

When the illness is prolonged or complications occur, myocarditis should be looked for and the necessary rest and avoidance of physical strain insisted upon. For *broncho-pneumonia*, sulphonamides, penicillin and aureomycin or chloramphenicol have their special indications and laryngeal swabs, blood and sputum should be cultured for the secondary organism and its sensitivity to the various drugs determined. In pure virus pneumonia and in all severe pneumonias in young children, the oxygen tent is remarkably helpful. It not only promotes oxygenation but tends to rest and quietness. For *herpes labialis* local application of ether by means of a pipette at the earliest stage is rapidly curative. It aborts the evolution of this lesion. In convalescence any persistence of bronchitis or of X-ray evidence of patchy pulmonary collapse or infiltration requires prolonged dieto-hygienic treatment ; such cases should remain under supervision until all danger of bronchiectasis seems over. A blood count will often reveal secondary anæmia. Large doses of iron and ammonium citrate mixture or of ferrous sulphate along with multiple vitamin preparations are then indicated.

[1] A good formula is :

Ephedrine hydrochlor.	0·50
Disodium hydrogen phosphate	0·35
Potass. dihydrogen phosphate	1·00
Dextrose	0·50
Phenyl mercuric nitrate (1 in 20,000) to	100·00

Prophylaxis. *General.—Instruction of the public* in the prevention of spread of infection is important, *e.g.* voluntary isolation from crowds during the infectious stage, restraint of coughing, sneezing and kissing, use of the handkerchief while sneezing and coughing, hygienic disposal of nasal exudates and sputum. Gauze masks with a paper or cellophane inter-lining, used in the early acute stage, reduce infectivity, but there are many objections to them on the wearer's part. In practice, their use is limited, *e.g.* to nurses and others in hospital wards and to a relatively short period. *Avoidance of exposure to wet and cold*, direct draughts, volatile irritants, dust, fatigue and other excesses is an ideal, and these things, if inevitable, should be neutralized by warmth, comfort and rest. Keeping feet warm is particularly important. Sterilizing the air of public places by volatilized propylene glycol and other highly diluted aerosols has achieved some success, but is difficult to carry out in practice. Irradiation of the air by ultra-violet light has given irregular results, tending to be negative in virus affections.

Local measures.—In normal persons, gargles, sprays, nasal douches, etc., cannot be recommended.

Active immunization by vaccines.—Some progress and much disappointment have to be recorded in this field. Andrewes (1939) used living attenuated virus, and Horsefall and others (1941) used formolized virus A vaccine combined with the virus of distemper. These have been superseded by vaccine of the type of Francis' virus A and B suspension obtained from the growth in chick embryo and concentrated eight- to ten-fold by the Hirst technique (Hirst *et al.*, 1944). The latter process consists of absorbing the virus to chicken erythrocytes followed by elution in a volume of fluid smaller than the original suspension. When such a vaccine was injected subcutaneously in man, and the level of antibody so produced was estimated during an epidemic in the United States in 1943, four important practical points were determined (Salk *et al.*, 1945 ; Francis *et al.*, 1945) : (1) that an inactivated formolized virus is as effective an antigen as living virus, (2) that one single injection produces as good a rise in antibody as several doses do, (3) that the rise in antibodies is greater with low than with high pre-inoculation titres, and (4) that the antibody response is of relatively short duration ; titres drop considerably after three or four months, but the vaccine may have a significant effect for a year after inoculation.

Considerable experience with influenza virus vaccine has been obtained in the U.S. Army. The Commission on Influenza (1944) reported the following findings.

Reactions.—Local redness and infiltration common but severe reaction limited to about 7 per cent. General reactions very infrequent.

Protection against influenza.—The morbidity of influenza in the inoculated was reduced by three-quarters as compared with the controls. The severity of attack in the inoculated was, on the whole, less than in the controls.

Antibody response.—In the case of virus A, this is marked and of the same order as that caused by the natural infection. Titres of antibody

above a certain critical level, whether naturally or artificially produced, are protective against clinical influenza. Critical titres are from 1 in 500 to 1 in 1,000.

Duration of immunity.—Study of experimentally induced influenza infection in inoculated subjects showed that protection is established about eight days after inoculation, has diminished four and a half months later for virus A but not for virus B, and is not completely exhausted after one year.

Field studies since 1943 with this type of mixed A and B vaccine have been somewhat disappointing. It gave protection during an influenza B epidemic but entirely failed to protect during various influenza A outbreaks in 1947. The A strains in this outbreak were then found to be antigenically different from the two A strains incorporated in the vaccine. It is now evident that influenza virus vaccines are unlikely to be successful unless they produce specific antibodies against the actual strain associated with each outbreak.

The use for many years of the so-called " influenza vaccines " or " cold vaccines " composed of the bacteria of secondary infection has provided no satisfactory proof of their efficacy.

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ACTINOMYCOSIS

Actinomycosis is a chronic infective granulomatous disease caused by the *Actinomyces bovis* or ray fungus, so called because of the radiate arrangement of filaments at the edge of the colonies of the organism. It is the commonest mycosis occurring in man but it is much more common in animals (horse, cattle, pig) where it gives rise to a local affection of the mouth, jaws or tongue (" lumpy jaw ").

The disease was originally recognized by Bollinger in 1877, who discovered the parasite in animal lesions. In 1879, J. Israel described the similar condition in man, and in 1891, Wolff and Israel cultivated the anærobic strain of the parasite which has become recognized as the classical species associated with the disease.

Ætiology.—*Actinomyces bovis* (Wolff-Israel type) is predominantly an anærobic organism and a strict parasite of man and cattle. Ærobic types of the genus are mostly saprophytic, although occasionally they are able to give rise to chronic granulomatous lesions in man, *e.g.* Madura foot. Topley and Wilson (1946) give a comprehensive classification of the *Actinomyces* group and of the various forms of actinomycosis.

In smear preparations *Actinomyces* appears as jointed and unjointed filaments some of which show true branching. In culture the Wolff-Israel type occurs chiefly as rods 3 to 4μ long by 0·6μ broad, many of them with clubbed ends ; but it is pleomorphic, and careful search will reveal branching filaments. The organism is gram-positive, non-motile and acid fast. It is killed by moist heat at 60° C. for fifteen minutes. Dried on glass and kept in the dark it may live for seven weeks or more. It grows at an optimum temperature of 37° C. and is strictly anærobic when first isolated. Colonies on glucose agar or Loeffler's serum are well developed in seven days. It is only slightly pathogenic to laboratory animals.

In the tissues it grows in the form of colonies which macroscopically have the appearance of greyish white or yellow (" sulphur ") granules, varying in size up to 1 mm. in diameter. These granules consist of a central mass of partly necrotic gram-positive filaments and a peripheral zone of gram-negative swollen club-like bodies arranged radially. The clubs are surrounded by pus cells and dense masses of fibrous tissue. The pus discharged from these lesions is not abundant. When it is shaken with water in a test tube, the granules separate and gradually sink to the bottom.

Mode of infection.—*Actinomyces bovis* of Wolff-Israel type has been shown by various workers (Naeslund, 1929 ; Slack, 1942) to be a normal inhabitant of the human mouth. It has been isolated particularly from salivary calculi, diseased tonsils, carious teeth and pyorrhœal pus. The mere presence of the fungus, however, need not precipitate an infection unless the tissue concerned is in some way devitalized, for example, by trauma or by bacterial or virus infection. The exact conditions leading to actinomycotic disease have not yet been clearly defined but there is evidence that symbiosis of certain bacteria and fungi has often a stimulating effect upon one another's growth, although occasionally the reverse is seen (Gohar, 1950).

The organism may thus gain an entrance to the tissues through traumatized abrasions or septic tooth sockets or other lesions providing the conditions for anærobic growth. The older view that it was introduced in the act of chewing grass is not tenable as the *Actinomyces* of grasses are of the saprophytic aerobic type.

Pathology.—Unlike tuberculosis or syphilis, actinomycosis does not involve the lymphatic system ; very occasionally, however, lesions are

found in lymphatic glands. The disease spreads by *direct extension*, starting in the sub-cutaneous or sub-mucous tissues ; exceptionally the lesion may rupture into a blood vessel, giving rise to metastases in liver, brain or heart. Gastro-intestinal lesions probably originate from foci in the mouth. They begin mainly in the caecum, appendix or œsophagus, but may spread widely to abdominal viscera, thoracic cavity and the trunk.

A granulomatous mass forms at the site of the infection. This has a peripheral zone of fibrous tissue, which in the cervico-facial lesions may be exceedingly dense. The centre of the mass softens with the formation of pus. This process is repeated, and so the lesion spreads. Involvement of the skin usually occurs with the formation of multiple sinuses. Secondary infection with other organisms is common.

The histological appearances are those of a granuloma, combined with suppuration. There is cell necrosis in the centre of the mass, with pus formation, in which are to be seen the " sulphur " granules. The living hyphæ are radially disposed towards the periphery, and some may possess terminal club-like swellings. Beyond this there is a dense zone of chronic inflammatory cells, giant cells, fibroblasts and fibrous tissue.

Symptomatology.—Actinomycosis may occur at any age, but it is rare in childhood. According to Cope (1938) less than 3 per cent. of cases are in children under the age of ten years. The youngest reported is in a twenty-eight-day-old infant who died with an actinomycotic pulmonary abscess. Ellis (1935) reported five cases in children : three were abdominal and two intra-thoracic.

There does not appear to be any significant difference in the sex incidence in children but adult males in rural districts, by virtue probably of their occupation, are much more affected than females.

The chief sites of infection in order of frequency are as follows :

(1) Head and neck.
(2) Ilio-cæcal region and appendix.
(3) Intra-thoracic.
(4) Skin.

In the neck a firm mass develops, surrounded by a brawny swelling. It eventually breaks down and becomes riddled with abscesses ; sinuses form between the lesion and the skin. The jaw is frequently eroded.

In the abdominal form of the disease, a firm mass forms in the cæcum or appendix ; suppuration ensues and sinuses are formed between it and the abdominal wall.

In the thoracic type a solid mass develops in the lung and slowly spreads until the greater part of the lung is affected ; there is a strong fibrous tissue reaction ; the chest wall may be invaded. In the mediastinal type, the lesion may originate in the œsophagus ; the parietes are early invaded and erosion of the vertebræ or ribs may occur.

Prognosis.—This is much more favourable in actinomycosis of the skin or superficial structures. The abdominal, thoracic and mediastinal types are generally fatal, although the outlook may be improved by the use of the newer methods of therapy.

Treatment.—Many drugs have been employed in the treatment of actinomycosis and it is not easy to assess their value. Since the disease was first recognized, iodine has been used. It is given, either as potassium iodide or tincture of iodine ; the former is often administered in very large doses to the point of tolerance, but it is doubtful if this is necessary. Chitty (1926) claimed good results with 5 to 10 minim doses of tincture of iodine, three times daily, in milk. Iodine salts have also been injected into diseased tissues, or given intravenously. In pulmonary actinomycosis, iodised oil has been injected into the bronchi.

Thymol is another drug for which successful claims have been made. Myers (1937) reported five cases treated with this drug.

The use of sulphonamides has been reported by Hollingbeck and Turnoff (1943), Miller and Fell (1940), Dobson *et al.* (1941) and Lyons *et al.* (1943). The drug was given for a period of several months in moderate doses ; the patient of Miller and Fell was a Negro boy aged eleven years with abdominal actinomycosis. He was given 0·65 gramme three times daily, for ten months. He gradually recovered. The action of sulphonamides is probably mainly a bactericidal effect against secondary invaders.

Actinomyces bovis is sensitive to penicillin *in vitro* though different strains seem to vary considerably in susceptibility. Dobson and Cutting (1945) treated three cases with penicillin alone ; one was cured and two arrested. All of Walker and Hamilton's (1945) cases responded well. Very large doses are required, viz. 1 to 3 million units daily over periods of from six to eight weeks. Arden (1945) treated a girl of ten years suffering from thoracic actinomycosis and the response was dramatic. There was no sign of recurrence five months after the cessation of treatment. In spite of these successes, sulphonamides and penicillin, even in combination, often fail. The newer antibiotics are more hopeful. A dramatic success with aureomycin, with complete disappearance of a sinus-riddled mass in twenty days, was reported in a case of actinomycosis of the face of six months' duration by Wright and Lowen (1950).

Surgical excision or amputation should never be used until antibiotic and other conservative therapy has been thoroughly tried out, and then only if the patients' survival is in danger.

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UNDULANT FEVER (BRUCELLOSIS)

Undulant fever is an illness caused by infection with the Brucella group of small Gram-negative cocco-bacilli. The majority of cases are characterized by relapses and remissions which produce undulant curves on the temperature chart. The disease is widespread, having a reservoir of infection in farm animals. It first attracted attention in Mediterranean countries and infection by *Br. melitensis* is known as Malta fever or Mediterranean fever. This variety occurs mainly in goats, and was isolated from the spleens of fatal cases of Malta fever by Bruce in 1887. In 1895 Bang showed that *Br. abortus* was the cause of infectious abortion in cattle in Denmark. Although American workers realized the possibility of human infection by *Br. abortus* and demonstrated its similarity to *Br. melitensis* (Evans, 1918), infection in man was not finally proved until 1924 (Bevan, 1921; Keefer, 1924; Orpen, 1924).

Ætiology.—Several types of Brucella have been identified. It is convenient for the physician to consider only three varieties:

1. *Br. melitensis*, occurring mainly in goats in Mediterranean countries. Human disease is usually due to the consumption of unboiled or unpasteurized milk, cream, and freshly made cheese.

2. *Br. abortus*, occurring mainly in cows in many parts of the world, and also producing human disease by the same infected dairy products. This is the least virulent of the three types.

3. *Br. suis*, mainly found in pigs in the United States and Denmark. It is not usually dangerous to children as infection is acquired by handling carcases, but cows and their milk can be infected.

The types may be identified by observing the effect of carbon dioxide and of dyes on their growth, and by agglutinin-absorption.

Type	10 per cent. CO_2 required	Growth inhibited by:		Type of agglutinogen
		Basic fuchsin 1/25,000	Thionin 1/50,000	
Melitensis	0	0	0	*Melitensis*
Abortus	+	0	+	*Abortus*
Suis	0	+	0	*Abortus*

In Britain undulant fever is caused by *Br. abortus*. No human cases of *Br. melitensis* or *Br. suis* have been detected in this country (Dalrymple-

Champneys, 1950). Although many cattle are infected the disease is uncommon in adults and rare in children. The reasons for this are not clear, but the absence of *Br. suis*, the rarety of herd infection with *Br. melitensis* and the low pathogenicity for man of *Br. abortus*, must be important. Pasteurization of milk kills the organisms.

The relative insusceptibility of young children is surprising. Dooley (1931, 1932) observed an outbreak in a school community using infected milk from a single dairy. Several adults had moderately severe attacks. Of over three hundred adolescent boys and young adults 41 per cent. developed agglutinins to *Br. abortus*. Of fifteen children under ten years old none developed either agglutinins or undulant fever. A parallel observation is that calves are not susceptible; definite infection is not established before sexual maturity.

Pathology.—There is nothing pathognomonic in the morbid anatomy, but complications such as bacterial endocarditis or meningitis may be seen. The basic lesion is an infective granuloma. Clinical pathology is more informative. *Br. melitensis*, and less often *Br. abortus*, may be isolated by blood culture at the onset of a febrile phase, and at times even during remissions. Growth is slow. A positive result will often be obtained in five to ten days, but it may be necessary to wait for two to four weeks and even to repeat blood culture daily for seven to ten days (M'Cullough, 1949). Bacteria have also been grown from duodenal bile, lymph glands removed at biopsy, synovial fluid, fæces and urine (Poston, 1941).

The *agglutination* test often becomes positive after five days but may remain negative for long periods. Furthermore, positive results have been obtained in from 2 to 23 per cent. of patients not suffering from brucellosis (League of Nations Report, 1930). The mere ingestion of infected milk for a considerable period can cause children to produce agglutinins without clinical illness (McBryde *et al.*, 1934). A rising titre is important, but intercurrent fevers may cause the titre to rise (anamnestic reaction) if the serum already agglutinates the organism in a low dilution (Dooley, 1932). In this disease, moreover, the "zone phenomenon" is important, that is, the existence of *zones* of negative agglutination usually preceding the positive zone but sometimes splitting it in two. In spite of these disadvantages the agglutination test is a useful aid to diagnosis, and the more complicated complement fixation and opsonocytophagic tests have no advantages over it except as confirmatory tests when agglutination is negative. A titre of $\frac{1}{60}$ is suggestive, $\frac{1}{100}$ diagnostic (Stitt, 1943).

The *intradermal test* with 0·1 c.cm. of an extract of a broth culture (brucellin) detects *sensitivity* to brucella antigens. The test is positive when a red œdematous plaque, 2 to 6 cm. in diameter and sometimes tender, appears in four to forty-eight hours. A simple erythema disappearing in twenty-four hours is regarded as negative. This is a useful test for retrospective diagnosis when other tests have failed. A negative result is strong evidence of the absence of brucella infection; a positive result merely indicates that the patient has been sensitized either by

past or recent experience of brucella infection (Dalrymple-Champneys, 1950).

The *blood count* usually shows leucopenia with relative or absolute lymphocytosis, but the count may be normal and is occasionally raised. The large mononuclear cells are often increased. As the disease progresses anæmia is likely to develop.

Clinical feature.—The incubation period is two to four weeks in most natural infections by mouth. In the experiments of Morales-Otero (Dietrych and Bonynge, 1932) it was found to be ten to seventeen days in volunteers.

The picture presented by a child with undulant fever usually has no distinctive features. Often there is merely headache, *sweating*, and remittent or intermittent fever rising to 101°–103° F. in the evenings for ten days, and settling by lysis in another week. The diagnosis in such cases is made by blood culture or agglutination. In some, after a period of remission of anything up to two weeks, there is a recurrence of fever which rises progressively and then falls, the relapse lasting from one to three weeks. It may be repeated, and the process may go on for months. Quite often, however, the characteristic undulant course is absent, and irregular or even daily remittent fever may persist for weeks or months. Although the onset may be accompanied by rigors or by vomiting and diarrhœa, the child does not usually appear very ill at first. In prolonged cases exhaustion, wasting, and anæmia may become obvious. Sleeplessness and constipation are troublesome at times.

The liver and spleen are often tender and palpable, and there may be local or general enlargement of the lymphatic glands. Pains in the muscles and joints are common, and there may be effusions in the joints and tendon sheaths. They are painful and do not respond to salicylates, but subside without sequelæ.

There are many rare complications : bronchitis, pleurisy, pericarditis, bacterial endocarditis, osteitis, infection of the urinary tract, purpura, epistaxis and other hæmorrhages, roseolar, papular, erythematous and urticarial rashes, subcutaneous abscesses, meningitis and encephalitis have been described.

The illness may be considered to be at an end when the temperature has been normal for two weeks. Convalescence is often slow. Fatigu-ability, irritability and listlessness may persist for several weeks.

The ultimate prognosis in children infected with *Br. abortus* is good, although death occasionally occurs. In Mediterranean fever the mortality has ranged from 3 to 6 per cent.

Diagnosis.—An assured clinical diagnosis can only be made from the appearance of the temperature chart in an undulant case. The main thing is to bear the diagnosis in mind in any child who has prolonged fever, particularly if it is associated with heavy sweats, muscle and joint pains, or enlargement of the lymphatic glands or spleen. The diagnosis has then to be established in the laboratory. Undulant fever may easily be confused with other conditions. In the early stages enteric fever is simulated. The high fever and splenomegaly may also suggest malaria.

Pyrexia, anæmia, and pain in the joints suggest rheumatic fever. Tuberculosis is often suspected because of the fever, sweating, and wasting, or on account of lymphadenopathy. On this account, too, glandular fever and Hodgkin's disease must be considered. In the diagnosis of this puzzling illness the persistent efforts of the pathologist play the key part.

Treatment.—The general treatment is similar to that of any prolonged fever. Reports on the use of sulphonamides are conflicting; it is possible that, combined with blood transfusion, they are effective early in the course of the illness. Penicillin is ineffective, and Alexander (1946) states that little can be expected from streptomycin in this disease. The best results from specific therapy have been obtained with aureomycin and with chloramphenicol. With either of these drugs conspicuous success, sometimes dramatic, has been obtained in about three-quarters of the cases treated and rather doubtful or no benefit in the remainder. The dosage of either drug for children is 50 to 100 mgm. per kilo. body weight daily in three to six divided doses. The optimum duration of treatment is not yet determined. Relapses sometimes occur after apparent cure (Dalrymple-Champneys, 1950).

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CHAPTER XXXVI

DISEASES OF THE SKIN

REGINALD T. BRAIN

Introduction

Few skin diseases are peculiar to childhood, but most of the congenital anomalies affecting the skin naturally occur early in life and some of these conditions, by responding to treatment or disappearing spontaneously, cease to trouble the adult. Infections are more likely to run an acute course in children, and the parasitic diseases are increased by overcrowding and neglect. Children, especially infants, are largely dependent upon mothers and nurses, and the incidence of infections and parasitic skin diseases is a measure of the standard of hygiene.

A great deal may be learnt from careful examination of the skin. The epidermis represents the ectoderm from which develops the whole central nervous system, the appendages, hair, nails, sweat and sebaceous glands, the cornea and lens of the eye, the tooth buds, important parts of the special sense organs generally, and part of the pituitary gland, which regulates growth. So it is that some of the congenital anomalies of the skin are associated with defects of the other specialized descendants of the ectodermal cells. Moreover, the skin reflects emotional and nervous states by the mechanism of the vegetative nervous system controlled by the endocrine glands and manifest by vasomotor changes or altered function of the epidermis and its appendages. The condition of the skin also reflects the nutritional state of the individual and in wasting diseases is apt to be thin, dry, and inelastic. Often, avitaminosis is first evident by changes in the skin. Vitamin A deficiency may result in a dry skin upon which the follicles are prominent and horny and in severe cases resemble toad skin (phrynodermia). Vitamin A deficiency appears to be an occasional factor in light sensitivity of the skin. Certain diseases, mainly with follicular lesions, such as lichen spinulosus, Darier's disease, and some dystrophies of the hair and nails may respond favourably to full doses. The vitamin B complex contributes to the health of the skin, but although specific effects have been obtained from the use of the separate vitamin fractions, it is probably advantageous to administer the whole complex. Vitamin B_1 (aneurine) is not a specific for any particular dermatosis but it is used in the treatment of herpetic eruptions, the neurogenic dermatoses, lichen planus and alopecia. Vitamin B_2 (riboflavine) deficiency sometimes accounts for scaling and fissuring of the lips and angles of the mouth (perlèche) and may be of value in seborrhœic conditions. Nicotinic acid belongs to the vitamin B complex and is almost a specific for pellagra. It is also useful in herpes and may prove of value in skin lesions which are aggravated by light. Vitamin C deficiency, apart from obvious scurvy,

is suspected when eruptions become purpuric. It has been shown that some follicular eruptions of the acne type are related to a deficiency of ascorbic acid. Vitamin C appears to make the skin less susceptible to pyogenic infections and to assist healing and to inhibit toxic eruptions.

Vitamin D and calciferol (vitamin D_2, the synthetic product) ensure the absorption of calcium and thus may influence bullous or exudative skin lesions. Sometimes vitamin D appears to be a therapeutic substitute for ultra-violet light in such diseases as lupus vulgaris, acne, and psoriasis, which often respond favourably to actinic light in large doses. Calciferol is a specific in many cases of lupus vulgaris and the value of the pioneer work of Charpy, Dowling, and Prosser Thomas has been established, but toxic effects may be encountered.

Vitamin E (α-tocopherol) has been used with inconsistent results in lupus erythematosus, dermatomyositis, scleroderma and in other dermatoses thought to be secondary to degenerative changes in the vessels.

Vitamin K has to be considered as a possible factor in some types of purpura and may be effective in chronic urticaria.

Certain other metabolic disorders may be manifested by changes in the skin due to the deposition of calcium, cholesterol, amyloid, fat, or lipoid, or by pigmentary changes which may be the presenting sign of such diseases as pernicious anæmia, hæmochromatosis, or Addison's disease. Pigmentation may also be a sequel of therapy with arsenic, gold, mepacrine, phenolphthalein, silver, and other drugs.

The production of urticaria by the action of histamine will be mentioned, and there is increasing evidence of the importance of this substance in the itching which accompanies many dermatoses. A number of anti-histamine substances are effective in urticaria and may relieve the itching of eczema, prurigo, lichen planus, and the neuro-dermatoses.

Morphological terms.—The following is a brief summary of the descriptive terms employed in dermatology. The primary skin lesions may appear as *macules*, which are merely alterations in the colour of the skin, such as freckles or petechiæ. *Papules* are small elevations of the skin up to about ½ cm. in diameter; larger than this they are termed nodules, and larger still tumours. Papules are the common lesions of urticaria, lichen planus, and other toxic eruptions. *Vesicles* are small elevations of the skin, the size of papules but containing clear fluid; bullæ, blebs, or blisters are the terms given to larger lesions. A *wheal* or *pomphus* is an urticarial eruption, which, as shown by Lewis, is provoked by the liberation of histamine in the skin and represents what he describes as a "triple response" to any damage to the skin.

The so-called secondary lesions of the skin may be regarded as sequelæ of primary lesions; for instance, erythematous macules often become *scaly*, as in the case of psoriasis or pityriasis rosea, and vesicles almost invariably become *pustular*. As a result of damage to the skin small cracks may extend through the epidermis and expose the vascular dermis beneath forming *fissures* or *rhagades*. An *ulcer* is an inflammatory lesion in which the whole of the epidermis has been destroyed so that a scar is an inevitable sequel. *Scabs* and *crusts* are often used synony-

mously, but it is thought to be an advantage to retain the word crust for dried plasma and a scab for dried pus, so that the former is more characteristic of eczema and the latter of impetigo and pyogenic infections.

THE ANATOMY AND PHYSIOLOGY OF THE SKIN

The structure of the skin is illustrated by fig. 582 in which the epidermis is seen as the continuous outer layer of specialized cells which is maintained by the reproductive activity of the basal layer or *stratum germinativum*. This layer is not sharply separated from the true skin by a basement membrane but its cells send down protoplasmic processes resembling the fangs of molar teeth which securely anchor the epidermis to the dermis and ensure the intimate relationship between the two. In this layer pigment is often found and it is thought that some of the melanoblasts found in the dermis (and also nævoid cells, which are often pigmented) are derived from the basal cells of the epidermis, although Masson believed that pigmented nævus cells were of nervous origin. The cells of the " stratum germinativum " enlarge and divide to form daughter cells which are thrust outward by further divisions, and on their passage to the surface of the body they pass through a cycle of *prickle cells* and *granular cells* and ultimately become the flattened keratin scales of the *stratum corneum*. The hair and nails are keratin structures produced by a similar cycle of development from epidermal skin appendages, which also include sweat and sebaceous glands. The dermis, cutis, or corium is the name given to the subjacent tissue which supports, nourishes, and therefore largely controls the activity of the epidermis. Its outward surface is studded with minute processes termed the papillæ which interlock with the rete pegs of the epidermis, and contain fine capillary loops, lymph spaces, nerve fibres and touch corpuscles. Beneath the papillary layer of the dermis are the larger vessels and collections of elastic and collagen fibres which determine the toughness and elasticity of the skin, and support the sweat glands, their ducts and the hair follicles. In the subcutis are the larger vessels and adipose tissue.

The arteries supply the vascular tree and from its terminal twigs the venules return the blood to the corresponding veins. This vascular pattern accounts for the bright red macules of certain toxic eruptions when the toxin affects the arterial side of the capillaries and for the purple mottling of the skin (" livedo reticularis ") which results from venous congestion.

Functions of the skin.—Protection from moderate trauma and from infection is the most obvious function, and this depends upon an intact, healthy, horny layer. Bacteria are unable to attack the dry " stratum corneum " which usually has a slightly acid reaction inimical to their growth (*p*H 5 to 6).

The second important function of the skin is the regulation of body temperature, in which the sweat glands play a greater part than the capillaries. It is therefore desirable when the skin is hot and irritable not to prevent the evaporation of sweat by the application of grease.

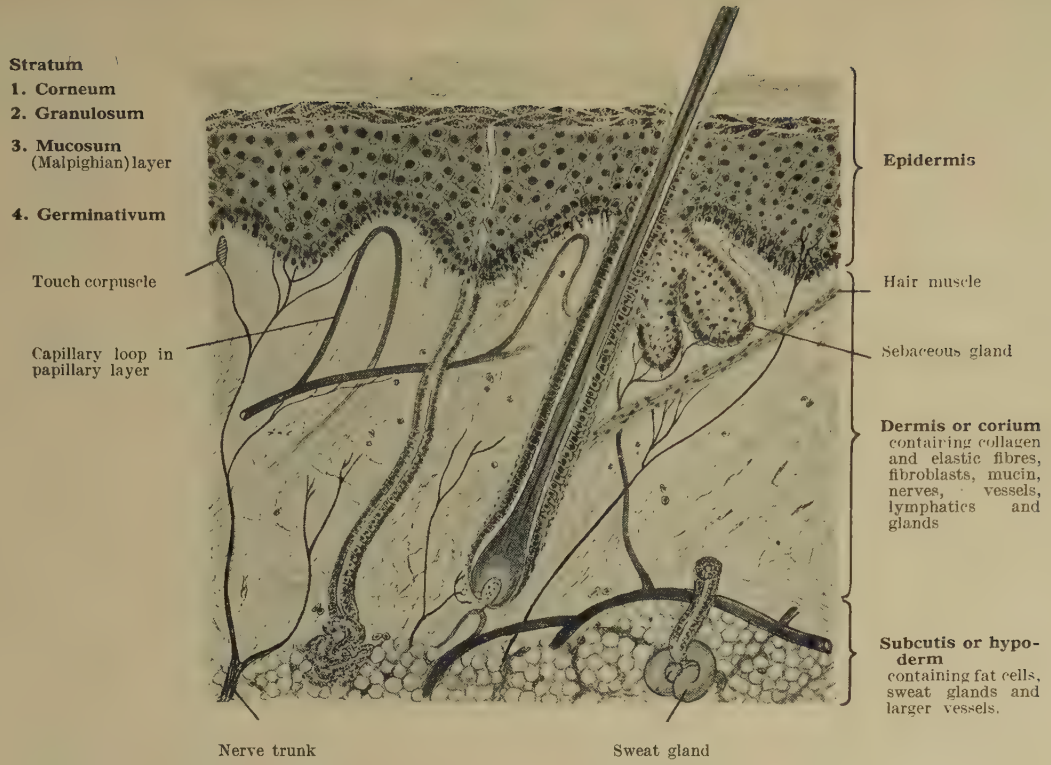

FIG. 582.—VERTICAL SECTION OF THE SKIN (DIAGRAMMATIC), INCLUDING PILO-SEBACEOUS FOLLICLE AND SWEAT GLANDS.

The sensory function of the skin largely determines its reaction to external factors. The fibres conveying the sensation of touch indicate the localization of parasites or noxious influences and these sensory fibres activate the scratch reflex. Itching (pruritus) is probably compounded from the sense of touch and the sense of pain, and these sensations reach the cortex via the thalamus. Excretion and secretion, which can scarcely be differentiated, are two functions performed by the sweat and sebaceous glands.

A further function of the skin is absorption, most exercised perhaps in the case of ultraviolet light when the irradiation is utilized for the production of vitamin D in the skin. Water and vegetable oils are taken up by the skin and certain drugs such as mercury, sulphur, and iodine are readily absorbed, but almost entirely through the sebaceous follicles.

GROUP 1—CONGENITAL ABNORMALITIES OF THE SKIN

(Xerodermia and ichthyosis—congenital ichthyosiform erythrodermia—dermatitis exfoliativa neonatorum—xerodermia pigmentosum—epidermolysis bullosa—ehlers-danlos syndrome—pseudo-xanthoma elasticum—nævi—neurofibroma—adenoma sebaceum—xanthoma)

Xerodermia.—The commonest congenital abnormality is xerodermia or " dry skin " which, in severe degrees, is associated with coarse scaling, the condition then being termed ichthyosis. In fact ichthyosis usually includes xerodermia, but the name is more aptly applied to the scaly anomaly, in which a wide range of hyperkeratosis occurs. In the most severe degree the newly-born infant is covered with thick, coarse scales and the term " harlequin fœtus " describes the effect. In this degree suckling is often impossible, and the state is not compatible with life. Xerodermia is undoubtedly an *ectodermal defect*, and under this latter title are described other more extensive abnormalities involving the hair as partial or total alopecia, the nails and the teeth. The latter are often widely spaced and undifferentiated, the milk teeth being late in erupting and incomplete, and sometimes the permanent tooth buds are absent. Congenital cataract and mental deficiency complete the gross ectodermal defect.

In xerodermia there is a relative absence of sweat and sebaceous glands so that the skin is too dry and the patient is unable efficiently to regulate body temperature when exposed to heat. These subjects are therefore unsuitable for tropical countries, although mild cases have a softer, more normal skin in warm weather because what glands they have are more active. The clinical picture varies from simple dryness to a coarse scaling of the skin which, becoming discoloured and imprisoning dirt in its interstices, gives the patient a dirty, neglected appearance. The parents are sometimes unfairly charged with neglect of the child's hygiene on this account.

Treatment is mainly palliative. In cold weather an oily liniment consisting of 25 per cent. liquid paraffin in a simple vegetable oil is far

better than an organic oil alone because the hydrocarbon is not absorbed by the skin. White soft paraffin rubbed into the skin after a hot bath may be more effective than paraffin or a simple oil if the skin is very dry. In warm weather a 25 to 30 per cent. glycerine solution may be used instead of the oil. Small doses of thyroid may be given in cold weather for, by increasing metabolism, the diminished sweat glands are rendered more active. It is undesirable to continue this endocrine stimulus indefinitely and it should be recognized that the true congenital anomaly is a structural defect which cannot be cured.

FIG. 583.—ICHTHYOSIS.

In minor types of xerodermia, especially when developing some time after birth, it is thought that vitamin A, hydrochloric acid, and iron are of value in treatment. Xerodermia predisposes to eczema and is common in Besnier's prurigo, which facts support the view to be expressed later that a congenital factor may be important in infantile eczema.

Congenital ichthyosiform erythrodermia is a rare disease, one type occurring at birth and the other later in life. The earliest sign is a generalized erythema, more or less intense, disappearing altogether in time. Thickening and ichthyosis may be present with the erythema, but usually develop later and, unlike simple ichthyosis, involve the

flexures. Bullous lesions may appear in cold weather. Areas of skin may be thin, absent or retracted, causing ectropion, limitation of movement of the digits and cicatricial alopecia (Cockayne, 1933).

REFERENCE

COCKAYNE, E. A. (1933). *Inherited Abnormalities of the Skin*, London.

Dermatitis exfoliativa neonatorum (Ritter's disease) is a rare disease of infants occurring within a few days to a few weeks after birth. Red exfoliating patches appear on the face or body and rapidly extend until the erythema and peeling are universal. Vesicles and bullæ may appear early and closely simulate pemphigus neonatorum of which disease it may be a variety, for some observers have isolated staphylococcus pyogenes aureus. The disease may also be confused with the bullous or the exfoliative dermatitis lesions of congenital syphilis.

FIG. 584.—XERODERMIA PIGMENTOSUM.
Showing pigmentation, atrophy and a pre-cancerous keratosis on the right cheek.

Leiner (1908) described a seborrhœic variety of generalized exfoliative dermatitis (erythrodermia desquamativa) which differed from Ritter's disease by the involvement of the scalp and by its more chronic course, but it seems probable that these diseases are merely clinical variants of pyogenic and seborrhœic dermatitis.

Xerodermia pigmentosum (Kaposi). This is a rare condition in which a dry skin is associated with an extraordinary vulnerability to light. Apart from the dry skin the infant may appear to be normal until exposed to bright sunlight and then an acute actinic dermatitis usually follows and the vesication occurring upon the erythematous areas may produce a picture of weeping and crusting, indistinguishable from an acutely inflamed facial eczema. Attacks may follow every year in the first bright sunlight of late spring and the diagnosis may not be suspected until conspicuous freckling marks the sites of reaction on the face and backs of hands and forearms. At first the freckles may fade in the winter, but soon they persist and small telangiectases appear and the mottling is increased by the appearance of white atrophic macules. Before the unfortunate patient reaches adolescence warty papules, which are essentially actinic keratoses, are likely to develop on the affected areas, and histologically these papules show a hyperplasia of a pre-cancerous type. Sooner or later one or more of the keratoses rapidly develops into a

squamous-celled epithelioma and as a rule, in spite of treatment, a fungating carcinoma with metastases causes a fatal termination in the second decade. The prognosis is, therefore, extremely grave, although the clinical course is variable and a patient in my care is now over sixty years and in good health, although she has been treated for more than a score of malignant growths of the skin.

The affection obviously presents similar features to the senile skin after prolonged exposure to tropical sunlight and also to chronic X-ray dermatitis.

Treatment. The reason for the skin's marked susceptibility to actinic light is obscure although it is known that the porphyrins can sensitize the skin to light and so can their related metabolites which are thought to be produced in the liver. Protection from bright sunlight

Fig. 585.—Epidermolysis Bullosa.
Showing epidermal cysts set in the discoloured sites of traumatic bullæ.

is essential and this may be achieved by the application of 10 per cent. tannic acid in 50 per cent. spirit or by an opaque lotion such as calamine lotion thickly applied. Yellow soft paraffin is a good protective for a dry skin. When warty papules appear they should be excised immediately for biopsy or treated by radium.

Epidermolysis bullosa may be considered here because, whereas xerodermia pigmentosa is the manifestation of the inability of the skin to tolerate actinic light, epidermolysis bullosa shows the inability of the skin to resist slight trauma. A trivial blow or slight friction may be followed by the development of bullæ. In severe degrees of the affection, friction between infant fingers may cause blistering and a knock against a pram cushion may produce a bleb an inch or more in diameter. By the time puberty is reached the recurrent blisters have often left reddened atrophic areas of skin over the knuckles, elbows, malleoli, and patellæ, and in these areas, which may superficially resemble psoriasis, small white epidermal cysts may be seen. At puberty a marked improvement may

occur, but in severe cases the disability persists into adult life. The soles only may be affected in mild cases. Rarely the bullous response to injury is delayed to the second or third decade. Many cases are inherited and occur as regular dominants in some families while in others a generation may be skipped. The diagnosis usually presents no difficulty, but when it occurs in the newly born the blisters may be mistaken for pemphigus neonatorum.

A rarer variety is epidermolysis bullosa hereditaria dystrophica in which familial cases of dominant or recessive type occur and bullæ arise on any part of the body, including the face, and instead of resolving may persist as granulomatous lesions, and even vegetate. Severe eye lesions from essential shrinking of the conjunctiva have been observed. The condition is ascribed to a defect of the elastic tissue or to a facile exudation from the vessels or to both. Treatment is palliative, and protective.

The Ehlers-Danlos syndrome is a rare congenital anomaly manifest by a syndrome including one or all of the under-mentioned peculiarities :—

(1) Undue fragility of the skin which permits a break in its continuity after slight trauma—*i.e.* the skin tears easily and bleeds.
(2) Varying degrees of elasticity of the skin which permit folds of skin to be drawn up away from the body.
(3) Laxity of ligaments allowing hyperextension of the smaller joints of the body, most easily demonstrable in the fingers.

Pseudo-xanthoma elasticum.—This rare condition which, appearing early in life, may be regarded in many cases as a congenital anomaly, bears some resemblance to the preceding disease. The skin is often soft with a doughy consistency and may be lax, in folds, or unduly extensible. The visible lesions are seen as flat, oval, shiny papules, yellowish or ivory in colour, in size from 1 to 5 mm., but sometimes aggregated into irregular plaques. The sides of the neck, the axillæ, groins, elbows, and lower abdomen are the sites usually affected. The disease is probably a degenerative condition affecting the elastic tissue, for microscopically the elastic fibres in the middle and deep parts of the corium are broken and patchy in distribution and there is a moderate infiltration with inflammatory cells. In later stages calcium is deposited in the corium and has also been seen in streaks alongside the larger veins. Angioid streaks are usually present in the retina. The disease may not affect the general health of the patient. Its cause is obscure but as in the cases of the two preceding conditions the elastic tissue is involved. Cockayne reviewed the incidence of familial cases and concludes that the condition is recessive to the normal and partially sex-limited to the female.

Nævi or birthmarks comprise a large group of common congenital abnormalities of the skin. They are obviously developmental and when extensive may be associated with other congenital defects. The cause is unknown, but it would appear certain that many of these defects occur so early in embryonic life that maternal impressions and influences are of no importance ætiologically. Vascular nævi are the most common and may involve blood or lymph vessels, the latter being relatively rare.

Hæmangiomata occur as flat pink or red marks, sometimes being deeply coloured (*e.g.* nævus flammeus and the port-wine mark). These macular lesions are the result of a coarse pattern in the superficial capillaries, whereas when the deeper vessels and veins are involved a soft bluish or purple swelling is palpable and is described as a cavernous hæmangioma. Mixed types, with superficial and deep elements, are not infrequent.

Treatment.—The superficial lesions will often respond to freezing with carbon dioxide snow applied with firm pressure for twenty to sixty seconds. An acute inflammatory response follows, and after six to eight weeks a further application may be given, but not more than two or three treatments should be necessary in skilled hands. Thorium-X is a painless method of treatment and may be more effective in the case of port-wine marks. An alcoholic solution of thorium-X containing 2,000 electrostatic units of radio-active thorium per c.cm. is painted on the pink areas every month. Treatment is more effective if the affected areas are first thoroughly cleansed with ether and after the painting are sealed with a thin film of collodion. The site should not be washed for at least a week after the application. The radio-activity of thorium-X is halved in approximately four days. After twelve to twenty applications considerable improvement is usually seen in the milder types of capillary nævus, but the port-wine marks are rather resistant and a perfect cosmetic result is rarely obtained by any method. The deep nævi disappear spontaneously with few exceptions, although they may not do so until the child reaches the age of five years. Therefore, when cavernous hæmangiomata occur in the scalp or on inconspicuous parts of the body they should be left alone. The best treatment is probably cautious irradiation avoiding any risk of subsequent atrophy; the response is slow, but the natural tendency to spontaneous disappearance is undoubtedly accelerated.

Fig. 586.—Capillary-cavernous Hæmangioma.

Lymphangiomata also occur as capillary or cavernous types. The former appear as groups of minute vesicles, the contents of which may become turbid after a fatty meal. Such lesions may be mistaken for herpes unless the history of their persistence has been obtained.

Treatment is very unsatisfactory and excision of the affected area of the skin is probably the most successful.

Pigmented nævi occur in all shades, from the palest brown to black.

Fig. 587.—Lymphangioma Circumscriptum.
Mostly pale yellow vesicles. A few coloured by hæmangiomatous elements.

Fig. 588.—Extensive Pigmented Nævus.

Lesions may be small or occupy large areas of the body. Many of the darker coloured nævi are also hairy. The paler lesions may be made less conspicuous by careful treatment with CO_2 snow or by painting with thorium-X. The darker ones, if small, may be completely excised for cosmetic reasons or left alone. Histologically many of the pigmented moles show collections of embryonic epidermal cells in the dermis; amongst them are melanoblasts. Although in the majority of cases the lesions remain benign, rarely rapid growth occurs, and a malignant melanoma is the result. It is probable that malignancy is already latent in such lesions so that any sign of growth is an immediate indication for complete and wide excision of the melanoma and microscopical examination. If malignant, metastases occur early, and often the most extensive surgery fails to save the patient.

Simple or fleshy moles are usually smooth, dome-shaped nodules which may include stout hairs. They may be excised or destroyed by diathermy or by electrolysis.

Fig. 589.—Adenoma Sebaceum (Pringle's Type).

Warty nævi may occur on any part of the body and are sometimes seen in the scalp as flat, pink areas, devoid of hair. Later vascular warty papillæ may develop and prove troublesome because of their tendency to bleed on trauma. Excision is the best treatment for this type. In other cases the warty lesions occur in lines or streaks which may extend from the sole of the foot to the groin or higher, and being limited, as a rule, to one half of the body they are sometimes called unilateral linear nævi. Pigmented nævi may also occur with a similar distribution.

Treatment.—If the warty lesions are small, and not extensive, they may be destroyed individually by diathermy. Otherwise excision of the whole linear lesion is the obvious method, and it is unfortunate that there appears to be an undue tendency to keloid formation in the scar. X-ray therapy as soon as possible after excision is therefore advantageous.

Von Recklinghausen's disease may present lesions suggestive of simple fleshy moles or of macular pigmented moles, but more prominent or pendulous tumours are apt to develop later.

Adenoma sebaceum (Pringle) may be observed in early childhood as a symmetrical eruption of small red papules at the sides of the nose and occasionally slightly pigmented nodular lesions similar to sessile neurofibromata occur on the forehead or other parts of the body. The lesions increase in number especially about puberty. Thickenings also

occur on the meninges or as dense gliomata giving rise to the condition termed "tuberose sclerosis" which may account for fits of an epileptiform type. Paler lesions, similar to adenoma sebaceum and arising on the central part of the face and occasionally on the limbs, may be *epithelioma adenoides cysticum* of Brooke. Balzer described a type of adenoma sebaceum with pale lesions.

Leiomyomata consisting of small tumours of unstriped muscle fibres may simulate the above, and often the diagnosis of these solid or cystic cutaneous growths will depend upon a biopsy.

Granulosus rubra nasi (Jadassohn) is a rare condition affecting the nose and adjacent parts of the face. The tip of the nose is cold, red, and congested with a tendency to hyperhidrosis, and scattered on the

FIG. 590.—NÆVO-XANTHO-ENDOTHELIOMA.

congested surface are minute reddish-brown or bright red papules which account for the granular appearance from which the affection gets its name. The condition usually begins about the tenth year and clears up at puberty.

Treatment should be designed to improve peripheral circulation, and X-ray therapy and an astringent lotion reduce the swelling and the colour.

Xanthomata are yellow nodules or tumours containing cholesterol and lipochrome and may occur early in life as a congenital anomaly or appear later without obvious cause or be related to hypercholesteræmia such as occurs in cirrhosis of the liver after hepatitis, in diabetes mellitus and in Hand-Schüller-Christian disease. The smooth, firm, yellowish papules and nodules of xanthoma tuberosum are readily recognized and usually occur on the extensor surfaces of the elbows and knees but may be diffusely spread over the trunk. The presence of xanthomata calls

for a careful investigation of lipoid metabolism for sometimes similar deposits are widely spread in many tissues and organs including the liver, spleen, lungs, brain and bones.

Occasionally in early infancy pigmented yellowish-brown nodules, plaques or tumours appear and are termed nævo-xantho-endotheliomata. An example is shown in fig. 590.

GROUP 2.—DISEASES OF THE NEWLY BORN

(PEMPHIGUS NEONATORUM—SYPHILIS—NAPKIN ERUPTIONS—SCLEREMA AND ŒDEMA NEONATORUM—SCLERODERMIA)

Many of the above-mentioned congenital abnormalities will, of course, be noted at birth and to these may be added the following diseases.

Pemphigus neonatorum, which is a variety of bullous impetigo usually occurs a few days after birth. Blisters develop quickly upon inflamed bases and the walls of the blebs are so thin that they rupture easily and so disseminate the infection. Peri-ungual lesions are common, and in severe cases large blisters with circinate edges may cover a considerable part of the body, the smaller lesions being on the limbs. When the eruption is extensive the prognosis is grave. The disease may be confused with epidermolysis bullosa, or syphilitic pemphigus.

ÆTIOLOGY.—Pemphigus neonatorum used to be regarded as a streptococcal infection but a hæmolytic staphylococcus aureus is usually responsible. Cultures should be made from fresh bullæ and any pathogenic bacteria isolated should be tested for sensitivity against the available antibiotics in case of need.

TREATMENT.—Treatment includes bathing the infant in normal saline plus 1 in 2,000 mercuric chloride and dressing the lesions with a drying antiseptic lotion, as is advocated in the treatment of impetigo (p. 1851). Systemic treatment with penicillin or some other potent antibiotic may be urgently necessary if local treatment fails to dry up the lesions. When epidemic cases of pemphigus neonatorum arise, careful swabbing of the throats of nurses and doctors to exclude carriers is indicated. Infants with pemphigus should be isolated under the strictest precautions.

Congenital syphilis.—The newly-born baby may present an eruption similar to pemphigus neonatorum but which is the earliest manifestation of congenital syphilis. The bullous syphilide is apt to occur on the face, the palms, the soles and about the genitals, although it may appear upon any part of the body. Paronychial lesions are common. Mixed up with the flaccid bullæ are reddish brown plaques or flat papules (fig. 591). The buttocks, the palms and the soles are often of a deep lilac red colour. When syphilis appears so early the wizened infant is usually riddled with spirochætes and has a feeble cry and an enlarged liver and spleen. The prognosis is grave. It should be remembered that congenital syphilis is a rare disease and most eruptions diagnosed as bullous syphilis are pemphigus neonatorum. Sometimes the infant is born apparently healthy but after four or six weeks begins to lose weight,

develops a sallow complexion and an eruption of well-defined red or copper-coloured macules, which are often extensive upon the buttocks, but which also affect the central part of the face, the palms and the soles. Involvement of the nasal bones and mucosa account for snuffles and a falling-in of the nasal bridge, and chronic fissures develop at the angles of the mouth. At the age of two or three years congenital syphilitics may develop condylomata of the anus and then, or up to the age of ten years, gummatous ulcerations may appear on the face. Since the lesions of congenital syphilis often affect the napkin area it is convenient to discuss the other common napkin eruptions here.

FIG. 591.—CONGENITAL SYPHILIS.
Compare with simple napkin erythema.

Napkin eruptions.—The common napkin eruption is that due to irritation of the skin by soiled napkins or by irritant cleansing materials used in washing the napkins. Another variety, a vivid erythema, is due to the burning of the skin with ammonia produced in the wet napkin by the bacterial fermentation of urea due to a saprophytic bacillus from the fæces. The condition can be prevented by giving the infant small doses of grey powder and by soaking the clean napkins in a strong solution of boric acid or in 1 in 2,000 mercuric chloride and then allowing them to dry. This type of napkin eruption is sometimes described as the erythema of Jacquet who described four varieties, simple, erosive, papular or post-erosive and ulcerative.

All varieties of napkin dermatitis are characterized by a superficial inflammation of the skin involving the convex surfaces, where the skin

is in most intimate contact with the napkin (fig. 592). The folds are not usually involved unless a secondary infection occurs and then a pus-coccal variety of intertrigo results.

Intertrigo may be classified into four types. The first is a simple inflammation involving the creases of the buttocks and the groins, which is the result of friction and moisture and usually of careless hygiene on the part of the mother or nurse. The second variety is due to pus-coccal infection and is seen as an acute inflammation with superficial fissures exuding plasma and becoming purulent. This pyogenic type is often associated with impetigo or chronic septic fissures on some other part of the body. A third type is a seborrhœic variety of intertrigo in which the inflammatory reaction is less acute and a soft, greasy scale is adherent to some parts of the inflamed folds. Evidence of the

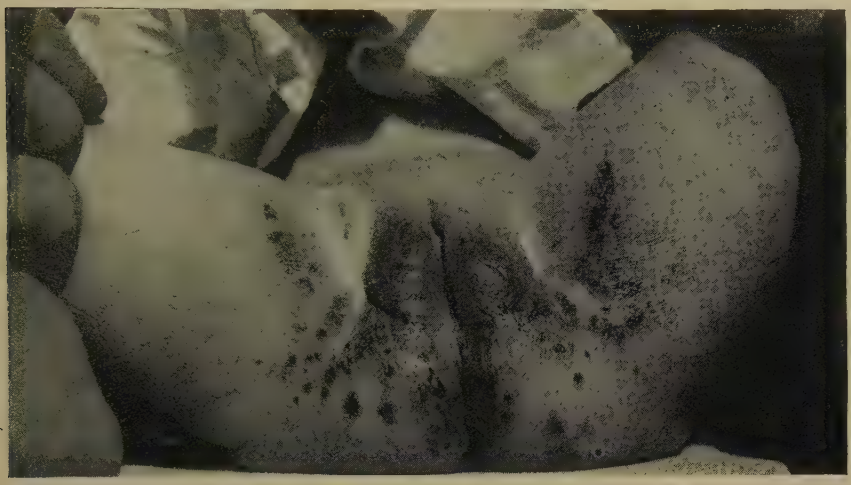

Fig. 592.—Napkin Erythema.

seborrhœic infection may be found in the scalp, behind the ears, and in other flexures. The fourth variety of intertrigo may be described as mycotic, since the causative organism is generally a yeast, monilia albicans (thrush) or monilia pinoyi. Buccal lesions are usually present when it is due to thrush and dull red scaly lesions may be found near the anus or in the gluteal cleft. Epidermophyton infections of the adult type are rarely seen in infants.

Sclerema neonatorum is a rare disease of the newly born developing within a few days or weeks after birth as a progressive hardening of the subcutaneous adipose tissue in well defined patches. The skin over the lesions is a purplish red colour and may appear to be harder and thicker because it is adherent to the indurated mass. Symmetrical lesions may be found on the buttocks, scapular and deltoid regions and also on the calves of the legs and on the cheeks. In the milder forms of the disease the infant's general condition may be unaffected and recovery is the

rule. The prognosis is bad in feeble infants who usually die of asthenia or gastro-enteritis.

Ætiology.—It appears that a diminished proportion of olein in the subcutaneous fat leads to the crystallization of palmitin and stearin or the glycerides of the higher fatty acids. A foreign body inflammatory reaction is then set up in the trabeculæ of the fat lobules and this produces the granuloma which constitutes the indurated swelling.

Treatment.—The infant should be kept warmer than usual and may be massaged with arachis oil to increase the olein fraction.

Subcutaneous fat necrosis of the new-born is probably synonymous with sclerema neonatorum, but some authorities believe it to be a

Fig. 593.—Sclerema neonatorum.

separate entity depending upon mechanical trauma or exposure to intense cold. The prognosis is said to be more favourable, but resolution of the indurated areas slower and may extend to three or four months.

Sclerema neonatorum has to be distinguished from the following:

(1) *The pre-agonic or cadaveric induration of the cellulo-adipose tissue* (Ballantyne) is caused by the solidification of the subcutaneous fat as the temperature falls in marasmic, moribund infants.

(2) *Œdema neonatorum* is a true œdema and the affected parts, usually the extremities and the eyelids, are pale on pressure although some induration may be present. It usually occurs in premature or feeble infants and if extending and associated with a subnormal temperature, often leads to coma and death.

(3) *Milroy's disease* or hereditary trophœdema is usually familial and affects one or both of the lower extremities, with a defined upper limit. The onset is sometimes delayed until puberty.

(4) *Sclerodermatomyositis*, a rarer disease of infants, occurs in older children as a more diffuse thickening of the skin and underlying muscles. Erythema and œdema of the skin, especially of the face, are the earliest

features. The skin may show some of the features of sclerodermia and the patient has febrile phases, muscular weakness, wasting and may develop contractures. Calcium may be deposited in the indurated, rigid muscles.

(5) *Sclerodermia*, also rare, does not differ from the adult type of the disease. The characteristic features are hardening of the skin progressing to atrophy and resulting in an ivory-like plaque. Older children are usually affected and the disease may be localized in small spots, bands or patches when it is sometimes called *morphœa* (fig. 594), or it may be diffuse, usually symmetrically, involving the limbs and trunk. If the extremities are affected the fingers and toes become stiff and atrophic, producing the condition called acrosclerosis or sclerodactylia. The early lesions of sclerodermia are often red or purplish, and being somewhat indurated may resemble sclerema, but the latter disease is more deeply set in the subcutaneous fat. No specific cause nor treatment is known, but resolution may occur spontaneously or the sclerodermia may persist in the localized variety or extend in the generalized type until wasting or broncho-pneumonia brings a fatal issue.

FIG. 594.—MORPHŒA (SCLERODERMA) IN THE AREA OF DISTRIBUTION OF THE SUPRA-ORBITAL NERVE.

The white area was smooth, shiny, with a feeling of stiff leather, and adherent to the skull.

(6) *Congenital syphilis* often presents discoloured, purplish red areas of skin, but when manifest in the newly born the disease is likely to produce bullæ and induration is uncommon. See page 1651.

GROUP 3.—DISEASES OF INFANTS AND YOUNG CHILDREN

(ECZEMA—SEBORRHŒIC DERMATITIS—DERMATITIS EXFOLIATIVA—LICHEN URTICATUS—URTICARIA PIGMENTOSA)

Eczema.—Eczema takes a prominent place in this group, and because it may appear within a few weeks of birth it seems likely that inherited qualities of irritability of the skin are of ætiological importance. Indeed, the way some infants react to external factors which are non-irritating to the normal skin suggests that the basis of the disease is a congenital anomaly, as definite as that seen in epidermolysis bullosa. However, there are two definite views upon the ætiology of eczema. Some authorities believe that external factors account for the whole clinical syndrome, whereas others believe constitutional or inherited qualities to be of fundamental importance. It is well to consider both, and while

endeavouring to discover any provocative allergen in the infant's diet or in its environment, attention should also be given to relieving irritation and mental stress, to promoting quiet sleep, and not least to educating the mother to understand her troublesome infant.

Clinical features.—Infantile eczema usually conforms to one of three clinical types. The first is a simple facial eczema in which the characteristic lesions of grouped, minute papulo-vesicles erupt on the sides of the face, usually on the malar regions and in front of the ears. In the early phase there is little or no erythema or diffuse inflammation of the skin which distinguishes eczema from an acute contact dermatitis.

Fig. 595.—Infantile Eczema (Facial Type).

Shows the characteristic mask-like distribution of the eruption on the forehead and cheeks, leaving free the nose and parts around the eyes and mouth. Note the grouped papulo-vesicles.

Rubbing, infection, or strong local applications produce a more defined dermatitis and aggravate the primary eczematous eruption, resulting in areas of weeping or crusted, eczematous dermatitis. The infant's discomfort increases with the extension of the eczema and auto-sensitization from the exudate appears to account for local spread. Absorption of the products of the damaged skin may at any time give rise to generalization, when symmetrical areas of eczema erupt on the limbs and may involve most parts of the body.

The second type of infantile eczema may be described as flexural, for the flexures of the arms, wrists, and backs of the knees are particularly susceptible. An intolerable irritation without visible lesions may mark the onset, and this disease is known as *Besnier's prurigo*. A family history of asthma, eczema, urticaria, or hay fever is common in this

variety and the subjects may at any time develop these other manifestations of allergy or atopy. It is this hereditary type of irritability of the epidermis which is so suggestive of some functional ectodermal defect and this view is supported by the failure to respond to treatment. Some of these patients have dry skins, so that instead of weeping the scratched areas become thickened, the skin pattern exaggerated by exudate and chronic infiltration with inflammatory cells, and the condition is described as *lichenification* (fig. 596). When the areas are well defined the terms *lichen simplex* or *lichen circumscriptus* are used. Usage condones some laxity in terminology here for neither Besnier's prurigo nor lichen simplex

FIG. 596.—FLEXURAL ECZEMA SHOWING THE CHRONIC LICHENIFIED LESIONS OF BESNIER'S PRURIGO.

is truly synonymous with eczema although the latter frequently erupts in either.

The third type of infantile eczema is that associated with a scurfy scalp. The first eczematous lesions are usually found in the scalp or near the scalp margin associated with a mild dermatitis in which the pink and exuding skin is covered with a soft, greasy scale. To this type the adjective "seborrhœic" may be applied. Although this does not imply that the eczema differs in any way from the other kinds, it is thought that the reaction of the skin is initiated by a mild infection derived from scurf and is therefore more likely to be responsive to local treatment. Unfortunately the seborrhœic subject is often unduly susceptible to infections and functional disorders. A child's own dandruff, or that of a parent, may be the offending allergen, and treatment of all the scurfy scalps in the family is indicated.

PATHOLOGY.—Although eczema is essentially an inflammation of the skin, the early lesions are focal and result from dilated capillary loops

in the dermal papillæ with exudation of plasma. The plasma produces œdema of the stratum mucosum and collects to form minute vesicles, either in the Malpighian layer or beneath the stratum corneum. The œdema and swelling of the prickle cells is described as spongiosis and the functional disturbance of the epidermis is shown by imperfect keratinization which leads to a mild hyperkeratosis and the presence of nucleated cells in the stratum corneum, which is termed parakeratosis.

FIG. 597.—INFANTILE ECZEMA. SEBORRHŒIC TYPE.

Note involvement of scalp and scaly lesions on temple and cheek. The eruption was widely spread on body and limbs.

DIAGNOSIS.—If the morphology of the early lesions is recognized the diagnosis of eczema rarely presents difficulty, but when a pyogenic or frictional dermatitis has been superadded the lesions may be indistinguishable from impetigo. However, the latter condition is rarely symmetrical unless secondary to eczema, urticaria, or scabies.

PROGNOSIS.—The mild cases will usually respond to treatment in a few months. The earlier the eruption appears, especially if associated with a familial history, the worse the prognosis. Besnier's prurigo is likely to give considerable trouble until puberty and even then to relapse if the skin is exposed to irritation or the subject to psychological stress. Infants with eczema who develop acute infections of the respiratory or alimentary tract are prone to sudden and unexpected death; they therefore require extremely careful nursing during these complications.

TREATMENT. *General.*—A properly balanced diet suitable for the age of the infant or child is a first essential, but it is rarely necessary to be faddy, and unless a child consistently reacts adversely to a certain food there is no indication to forbid it. In plump subjects starch and sugar should be restricted, and extra cream or rich Jersey milk is undesirable. Oatmeal and groats are better omitted from the diet of patients with eczema or urticaria. This cereal is regarded as overheating to the skin, whatever that may mean, but its unsuitability may

be due to an anti-vitamin D factor. The diet should be supplemented within reason by vitamins, and vitamins A, C, and D are usually given, but less attention is paid to the vitamin B complex which may be particularly useful to the nervous, irritable child. The therapeutic value of large doses of synthetic vitamins is doubtful. Alkalis appear to be useful in seborrhœic subjects and may diminish the irritability of the skin. Sodium citrate, 1 grain to each ounce of milk, may therefore be added, or given in a mixture such as the following in each feed :—

℞	Potassium bromide . .	1 grain
	Sodium citrate . . .	3 grains.
	Sodium sulphate . .	1 grain.
	Water to	60 minims.

When the child's breath is offensive and stools fermenting, 10 to 15 minims of dilute hydrochloric acid may be added to each feed, or in older children

Dilute hydrochloric acid .	15 minims.
Syrup of glucose to . .	60 minims

may be given with each protein meal and 5 to 10 grains of sodium sulphate may be added to the acid mixture for constipated children. Sedatives are often essential to secure rest and prevent further damage from scratching, and if small doses of bromide are not sufficient, phenobarbitone in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain may be given ; the drug is well tolerated by infants and young children but is certainly less effective than in adults, and chloral hydrate in adequate doses is often better. Small doses of acetylsalicylic acid or codeine compound tablets may be helpful and pruritus is sometimes relieved by antihistamine drugs which may be given as a palatable elixir even to infants.

Local treatment should be soothing and protective. The skin will usually tolerate cleansing with isotonic saline or with 1 per cent. sodium sulphate, either as a lotion or as a bath. It is a mistake to forbid bathing and to depend upon cleansing with greases which retain exudate and sweat on the skin and increase irritation and the tendency to sepsis. Local treatment must be conditioned to the phase of the eczematous eruption and careful watch should be kept for any signs of intolerance. Weeping lesions call for drying lotions and bland dusting powders. After gently removing exudate and crusts with isotonic saline one of the following lotions may be applied :—

(1) ℞ Glycerine 30 minims. (2) ℞ Coal tar solution 15 minims.
Lead lotion to 1 oz. Calamine lotion to 1 oz.
(3) ℞ Siccolam (B.D.H.)

One per cent. of the strong solution of lead subacetate in boiled milk is also well tolerated. If the lesions are infected, solutions of proflavine 0·1 per cent., gentian violet 0·5 per cent., or 0·1 per cent. of mercuric chloride in water are indicated. When the skin surface becomes too dry and cracks under lotions or when watery solutions aggravate, creams or pastes should be used. As a cream the oily calamine lotion may be used alone or to it may be added ichthyol 2 per cent., solution of coal tar 2 to 3

per cent., sulphur 1 per cent., or strong solution of lead subacetate 1 per cent. Alternatively the plain zinc paste may be applied, or Lassar's paste (which contains 2 per cent. of salicylic acid), and to either may be added 2 per cent. of ichthyol or of resorcin or of pyrogallol ; or 3 per cent. of crude coal tar or of yellow oxide of mercury. The modifications will depend upon the response of the patient and upon the presence or otherwise of infection and pruritus.

Finally, in the dry and lichenified phases the more greasy ointments of zinc, salicylic acid, phenol or coal tar may be indicated.

The introduction of emulsifying agents promises considerably to extend the usefulness and variety of the creams and ointments used in dermatology. The new bases readily incorporate the sweat and sebum and bring the medicaments more intimately into contact with the epidermis so that weaker concentrations are effective. Two B.P. preparations are available. The ointment of wool alcohols with 50 per cent. of water gives the hydrous ointment which is a water-in-oil emulsion. Emulsifying ointment will mix with water in all dilutions to yield oil in water emulsions. The hydrous emulsifying ointment contains approximately 70 per cent. of water. One or two ounces of emulsifying ointment creamed with water may be added as an emollient to the saline bath for the eczematous infant with a dry skin. Medicaments soluble in oil or insoluble in water are preferably added to ointment of wool alcohols. Hydrous emulsifying ointment is the vehicle for water-soluble substances.

Another type of emollient cream may be made from liquid paraffin 10 per cent., methyl cellulose 1·25 per cent., water to 100, and at The Hospital for Sick Children 3 per cent. of coal tar solution is added to this to make a tar cream. Whatever preparations are employed, thick dressings should be avoided because over-heating nearly always aggravates eczema. The patient is prevented from scratching by thin cardboard cylinders applied as splints, or by some device as illustrated in fig. 598, or by tying the wrists and ankles to the sides of the cot. Cotton or silk garments should be worn next to the skin, and contact with woollen coats should be prevented by silk facings. Occasionally small doses of X-rays, 30 to 50r, relieve irritation and may be repeated every two or three weeks for three or four doses. Brunettes usually tolerate ultra-violet light well and sub-erythema doses two or three times a week are good for the skin and for the child's general metabolism. In warm weather exposure of the naked skin to skyshine and moving air stimulates the normal physiology of the skin and makes it and its vessels less reactive.

Seborrhœic dermatitis.—This condition, which may occur very early in life, appears to be dependent upon either a scurfy scalp or an oily skin, but of course both may be present.

Scurf, dandruff, or pityriasis capitis is thought to be due to an infection of the stratum corneum with saprophytic organisms, amongst which the *Pityrosporon ovale* (the bottle bacillus) is constantly present. In mild degrees scurf is ubiquitous, and no doubt admiring parents and friends shed dandruff upon the newly-born and so infection occurs early. The healthy infant may show no more than a mild scurfiness of the scalp

Fig. 598.—Extensive and Infected Infantile Eczema showing the Restraining Bands as used in the Dermatological Unit of The Hospital for Sick Children.

which readily responds to cleansing with a simple oil and shampooing with soap in the bath. In other cases the dandruff is excessive and may require the application of an ointment containing 2 per cent. of salicylic acid and 2 per cent. of sulphur in coco-nut oil or in emulsifying ointment, B.P. When a preparation of this sort containing mild antiseptics is rubbed into the scalp the day preceding the shampoo, dandruff soon becomes inconspicuous but may recur unless the application is repeated for some time. Other children apparently become allergic to the organism and its products in the horny scales and patchy eczema then develops on the scalp or about its margins. This eruption, which may be termed seborrhœic eczema, has been mentioned previously and does not differ significantly from idiopathic eczema but may respond more readily if the scurfy condition can be cleared up permanently. Eczematous reactions to a parent's dandruff have been reported (p. 1833).

Seborrhœic dermatitis is recognized as a diffuse erythema covered by soft, greasy, yellowish scales. It is often patchy at first about the ears, forehead and nape of the neck, but may cover the whole scalp and is prone to produce a scaly intertrigo behind the ears or in the folds of a fat neck, and then it may involve the flexural surfaces of the arms, the axillæ, the navel, the groins, and account for one variety of napkin erythema. Sometimes seborrhœic dermatitis presents a circinate pattern which may be mistaken for ringworm, but the lesions are paler and show no vesicles or pustules in the margins and can usually be recognized as part of a more extensive eruption. In other cases the scaly areas show so little erythema that the lesions have been termed *pityriasis alba*. This condition differs little from the scaly variety of impetigo and because of this it is not generally accepted that seborrhœic dermatitis is due specifically to infection with the bottle bacillus, but may be caused by many of the common skin cocci. Probably the infecting organism is of less importance than the constitutional background or predisposition of the skin which makes the individual susceptible. The *p*H readings have been found to be above normal on seborrhœic subjects and doubtless the diminished acid reaction of the skin surface favours bacterial growth.

Diagnosis.—Seborrhœic lesions have to be differentiated from pityriasis rosea, scaly impetigo, eczema, and the milder ringworm infections, and the distinguishing features have already been mentioned.

Treatment.—The subjects are usually plump and overfed so that it is desirable to restrict starch, sugar, and fat and to increase the vitamin B complex, which not only ensures the complete oxidation of sugar, but probably has some effect upon scaly eruptions. Small doses of alkalies and sulphates may be helpful and nervous patients may require bromide or phenobarbitone. Woollen garments should not be worn next to the skin because unlike cotton garments they are not boiled in the laundry. Sodium bicarbonate or borax should be added to the bath, and as a rule soap may be used liberally to remove the greasy film which predisposes to the disease.

Local treatment consists in applying mild antiseptics and preparations containing sulphur or resorcin to the lesions. A lotion of 2 per cent.

precipitated sulphur in calamine is suitable for the hot surfaces and 2 per cent. of resorcin in Lassar's paste makes a useful application for the dry lesions. Ichthyol, 2 per cent. in oily calamine lotion and an ointment of precipitated sulphur and salicylic acid, 2 per cent. of each in emulsifying ointment, are also useful.

Acne vulgaris.—Acne vulgaris is rare under the age of puberty unless a patient is the subject of seborrhœa of some severity. The greasy skin itself may then give rise to comedones or pustular lesions but is much more likely to do so if not adequately cleansed with soap and

FIG. 599.—SEBORRHŒA WITH GROUPED COMEDONES IN AN INFANT AGED SIX MONTHS.

water. Cleansing with oil or the daily use of cold cream may account for acne in infancy which erupts as grouped comedones on the forehead, cheeks, or chest (fig. 599).

Treatment consists in keeping the skin surface free from grease and following the general measures recommended in seborrhœa. As a local application 2 per cent. of precipitated sulphur in calamine lotion is satisfactory, and exposure to sunlight and open air is valuable.

Lichen urticatus or **strophulus** is another common affection of infants and young children. It may begin with dentition or arise later, particularly when the patient is erupting some of the larger teeth. It is thought that some mild gastro-intestinal disturbance is the probable cause, but no obvious signs may be found. It was first shown by Hallam

and later confirmed that, as a rule, children with papular urticaria lose their eruption on admission to hospital, even if their food is brought from their homes. Further investigation appeared to show that in such circumstances relapse in hospital could be brought about by contact with dust brought from the patient's home; but there is little to be said for treating patients with this disease in hospital if they are likely to relapse on returning home.

The eruption consists of shotty papules which may be pale or pink, and are usually most numerous on the limbs but may occur on the loins and about the waist girdle. Occasionally a more obvious urticarial wheal may be distinguished amongst the papules and sometimes the papules are vesicular and may be bullous. Bullous lesions are usually more marked on the palms and soles, but blisters up to an inch or more in diameter have been seen on the limbs. The base of the blister is not usually inflamed so that the lesions are readily distinguished from bullous impetigo, and since dermatitis herpetiformis and pemphigus vulgaris of the adult type are rare in children these diagnoses need seldom be considered. Generalized fine papules characterize Besnier's prurigo and itching is intense. Infection of urticarial vesicles and bullæ is not so common as in the bullous lesions of scabies but it does occur, and then the symmetrical pustular eruption may be mistaken for varicella or variola, but the absence of a constitutional disturbance should exclude the specific fevers without difficulty. Itching is usual, but the symptom varies a good deal.

Treatment.—It is usually advantageous to restrict starch and fat, especially fried bread, bacon fat, pastry, boiled puddings, porridge and chocolate. Vitamins C and D and vitamin B complex are especially indicated, but large doses rarely have any specific effect. Small doses of grey powder and alkalies usually clear the eruption in a few weeks, but the nervous child may also need fractional doses of phenobarbitone at night and ephedrine hydrochloride $\frac{1}{8}$ grain may be given with it. An antihistamine drug may relieve itching although often without effect upon the eruption.

Locally, 2 per cent. of phenol in calamine lotion is satisfactory. Alkaline baths with carbolic or coal tar soap also relieve irritation. In obstinate cases general ultraviolet light therapy has been beneficial.

Urticaria pigmentosa is a rare affection which has been noted at birth but usually occurs in early infancy. The eruption may appear as pale brown macules or as somewhat darker nodules, involving the whole body, usually less prominent on the limbs. Striking variations in the size of lesions and in their distribution have been noted. The earliest lesions are erythematous or urticarial and later the redness darkens to a brownish shade, which then persists for several years at least.

A conspicuous feature of the histology is the presence of mast cells; in fact the nodular lesions may be regarded as mast cell tumours, and because of this it is thought that the eruption is a peculiar type of nævus. However, the eruption has undoubtedly arisen in adults up to the age of sixty years and it is rather difficult therefore to accept

this view as entirely satisfactory. Until more is known of the function of the mast cells the ætiology of urticaria pigmentosa will probably remain obscure. Apart from transient irritation in the early urticarial

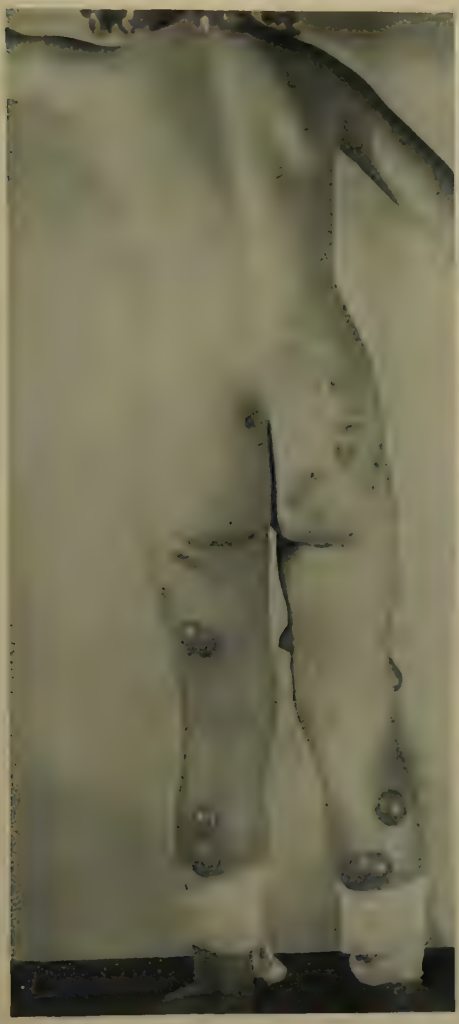

Fig. 600.—Lichen Urticatus, Bullous Lesions, and Shotty Papules.

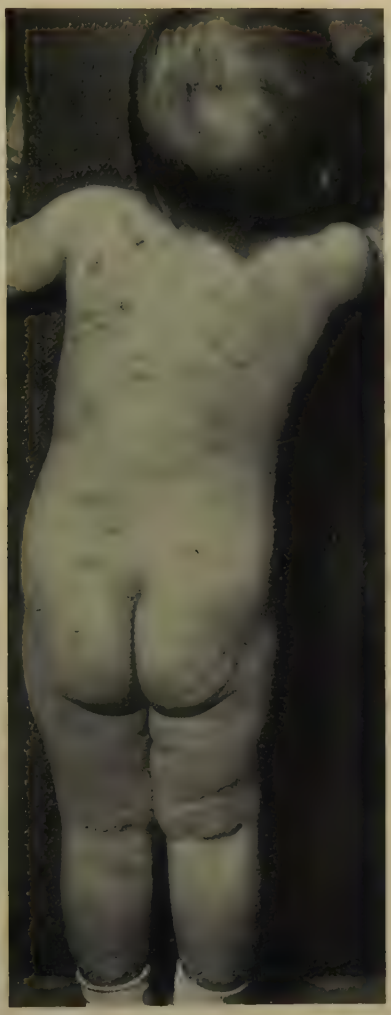

Fig. 601.—Urticaria Pigmentosa.

phases there are no symptoms, and no constitutional disturbance is associated with the eruption.

Treatment.—No specific treatment is known to influence the disease, but some of the measures mentioned as useful in urticaria may be applied for the relief of irritation.

GROUP 4.—SKIN DISEASES DUE TO INFECTION

(1) *With Animal Parasites.*
SCABIES—PEDICULOSIS.

(2) *With Fungi or Yeasts.*
TINEA CIRCINATA—TINEA VERSICOLOR—TINEA CAPITIS—FAVUS—TINEA UNGUIUM.

(3) *With Pus-cocci.*
IMPETIGO CONTAGIOSA—PYOGENIC DERMATITIS—BOCKHART'S IMPETIGO—MULTIPLE SUBCUTANEOUS ABSCESSES—BOILS—GANGRENE—DERMATITIS VEGETANS—PYOGENIC GRANULOMATA—ERYSIPELAS—ERYSIPELOID.

(4) *With Tuberculosis.*
LUPUS VULGARIS AND LUPUS VERRUCOSUS—TUBERCULIDES—LICHEN SCROFULOSORUM—PAPULO-NECROTIC LESIONS—ERYTHEMA NODOSUM—LUPUS ERYTHEMATOSUS.

(5) *With Viruses.*
HERPES—ZOSTER—VACCINATION ERUPTIONS AND VACCINIA—KAPOSI'S VARICELLIFORM ERUPTION—DERMATITIS HERPETIFORMIS—PEMPHIGUS VULGARIS—VERRUCAE—MOLLUSCUM CONTAGIOSUM—ORF.

Eruptions due to Animal Parasites

Scabies.—Scabies is a common disease of infants and children resulting from infection with a parasite called the *Sarcoptes scabiei*. It is characterized by the development of intense itching, especially when the skin is warm and so it is sometimes called "the itch." (An excellent account of the disease is given by Mellanby in a monograph published by the Oxford University Press, 1943, "Scabies.")

The adult female is just visible to the naked eye, being about $\frac{1}{60}$ of an inch in length with an oval body, flat below and convex above. It has four pairs of legs, the anterior pair ending in minute flappers, the posterior pair in long bristles. The adult male is about half the size of the female. A fertilized female is able to move rapidly on the warm surface of the skin and tunnels into the horny layer, taking about an hour to conceal herself. She then progresses along a little burrow depositing ova and excreta and occupies a minute vesicle at the advance end of the burrow where she can be seen with a watch-maker's lens. The ova take three or four days to hatch and the larvæ emerge to find shelter in neighbouring hair follicles. According to Mellanby, irritation does not develop until about a month after infection, and it is not due to the active movements of the burrowing mites but to an acquired allergic response to their products and to those of damaged follicles.

The eruption of scabies consists of burrows and discrete minute follicular papules affecting the whole body and limbs but usually most marked on the palms, the ulnar border of the hands, the creases of the wrists,

the inner aspects of the forearms, about the elbows, the anterior axillary folds, about the navel, the creases of the buttock, the thighs, the legs to the ankles and soles of the feet. On the palms, wrists, soles and ankles and sometimes about the elbows, burrows may be recognized, but in infants the response to the adult female acarus is often a larger vesicle or blister. The penetration and undermining of the horny layer facilitate infection, so that pustular and impetiginous lesions are apt to develop quickly and to obscure the basic infection. The face is seldom infected, except in suckling infants. Eczema is also prone to develop, either as a result of the infection and scratching or as a sequel to treatment with the stronger insecticides.

Fig. 602.—Scabies (Impetiginized).
Note lesions in palmar creases, folds of wrists and nates.

Diagnosis.—A generalized itching eruption in infants and children should be regarded as scabies until a careful examination has excluded the possibility. Symmetrical septic lesions, especially pustules on palms and soles, should also be regarded as probably due to scabies. Careful search should be made for burrows in the sites indicated and the presence of a typical burrow leaves no doubt as to the diagnosis. However, confirmation is readily obtained by moistening the burrow with liquor potassæ, scraping it out thoroughly, and examining the scraping with the low power of a microscope. The presence of an acarus or of one ovum establishes the diagnosis beyond doubt (fig. 603). When bullous or pustular lesions are prominent a burrow may not be found and then the parents should be examined, because it is probable that other members of the family are infected and burrows may be more characteristic in the adult than in the infant. A vesicular or bullous

lichen urticatus is most likely to give difficulty in diagnosis and at times it is impossible to be certain, but sepsis occurs earlier and it is usually more marked in scabies than in urticaria. Occasionally an extensive eczema, particularly of the Besnier's prurigo type, closely imitates scabies, when multiple discrete lesions (the papules of prurigo) imitate the acarine follicular papules.

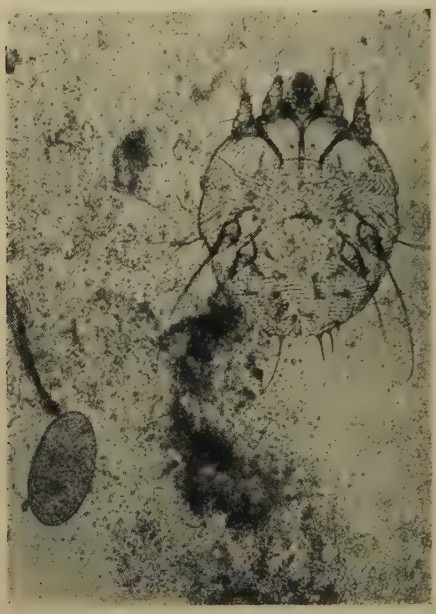

Fig. 603.—Scabies.

The result of a scraping from a burrow on the hand. Adult female acarus and ovum.

Treatment.—The usual method now advocated is to give a hot bath with a thorough soaping to soften the horny layer protecting the acarus and its eggs and then to paint the whole body, not forgetting the palms and soles, with an emulsion containing benzyl benzoate. Twenty per cent. of benzyl benzoate is an adequate strength for children and it is not uncommon for the emulsion to produce severe discomfort, with a burning sensation and sometimes dermatitis or eczema. If the child becomes distressed the application should be removed by a hot bath and the skin cooled by the application of calamine lotion to which 2 per cent. of precipitated sulphur may be added. If further treatment is required, 12 per cent. of balsam of Peru in zinc ointment may be tried or half strength sulphur ointment, or a mixture of equal parts of these two ointments. Any subsequent irritation of the skin, eczema or dermatitis, will usually respond to the treatment advocated for eczema. It is essential that all members of the family should be treated whenever possible, or at least those who develop any symptoms suggesting infection. Although the risk of re-infection from clothing and bedding is almost negligible, it is desirable on hygienic and psychological grounds to have the next-to-skin clothing disinfected and the sheets boiled. Periodic examinations should be made to ensure that no relapse or re-infection from an undiscovered contact occurs.

Pediculosis.—Pediculosis capitis is common in poor children. The infestation should be suspected whenever a child presents impetiginous lesions and excoriations about the neck and across the shoulders, and it is a condition to be excluded in the differential diagnosis of enlarged cervical glands. Extensive impetigo of the scalp may obscure the primary disease, but as a rule careful examination with a hand lens reveals the presence of "nits," the ova of the head louse. These small

bodies are firmly cemented to the hair shaft and appear as little goblets, grey and translucent, until the larval insect has emerged, when they become shrunken and silvery. They may on superficial examination be readily confused with scurfy scales, but the latter are easily detached by stroking with the finger-tip, whereas the ova do not move. Combing with a fine tooth-comb extracts the living lice which can be seen without visual aids if they are allowed to fall upon a piece of white paper.

Treatment is usually simple, for the insects are rapidly destroyed if covered by oily films which obstruct their breathing Camphorated oil or 20 per cent. of crude paraffin (kerosine) in a simple oil, or 1 in 40 phenol solution applied liberally to the scalp with frequent shampoos, using an abundance of carbolic soap, rapidly destroys the living parasites and many developing ova. A few weekly treatments will deal with subsequent hatchings, and it is quite unnecessary as a rule to cut the hair or to comb out the nits; the latter procedure requires an expensive special comb and is tedious and uncomfortable. With the development of modern insecticides more active preparations are available, and "lethane" hair oil has been recommended by the authorities for the treatment of pediculosis capitis: about 30 to 60 minims of the preparation are applied carefully to the whole scalp and left for about a week, when all the parasites and the ova will have been destroyed. Unfortunately, liberal use of this preparation and the enclosure of the scalp has occasionally given rise to serious toxic sequelæ.

Pediculosis corporis is rarely seen in children unless they are very neglected. The diagnosis should be suspected when an eruption limited to the trunk is somewhat suggestive of scabies and that diagnosis is excluded. The parasites should be looked for in the seams of the underclothing, and treatment is based on the usual hygienic principles. D.D.T. powder is a specific in treatment and in prophylaxis.

Pediculosis pubis does not occur in children unless they show premature sexual development with the adult type of hair, but the insect may infest the eyelashes, and rows of nits may be seen at the bases of the hairs, producing a darkening of the eyelid margins. The parasites may be destroyed by the daily application of yellow oxide of mercury ointment.

Flea bites, caused by pulex irritans, are usually recognized because the irritation is immediate and the parasite may be seen. The lesions appear as bright red spots indicating the bite, and these spots are apt to occur in little groups. They may be mistaken for the smaller lesions of purpura but are more often urticarial.

Bug bites due to cimex lectularius may be numerous on the newly born, but subsequently the frequently-bitten subjects develop a degree of immunity which results in the lesions becoming smaller and less troublesome in course of time. The lesions occur as indurated, red papules, in the centre of which the small bright red depression of the bite of the insect may sometimes be recognized. Irritation is intense and the itching papule may persist for a week or longer. Bedbugs

usually bite at night and escape to their hiding-places in crevices of bedsteads, in the seams of mattresses, or behind wallpaper, pictures and wainscotting. Mild infestations often escape detection until careful searches are made in the middle of the night.

Gnat bites and the red, irritating follicular lesions caused by harvest bugs and mostly affecting the lower extremities, usually give no difficulty in diagnosis.

Urticarial lesions and severe conjunctivitis may result from touching hairy caterpillars.

Fungus Infections

Ringworm or **tinea circinata** is the term applied to a fungus infection of the skin. The usual organisms are the microsporon Audouinii, which accounts for the majority of cases of ringworm of the scalp in

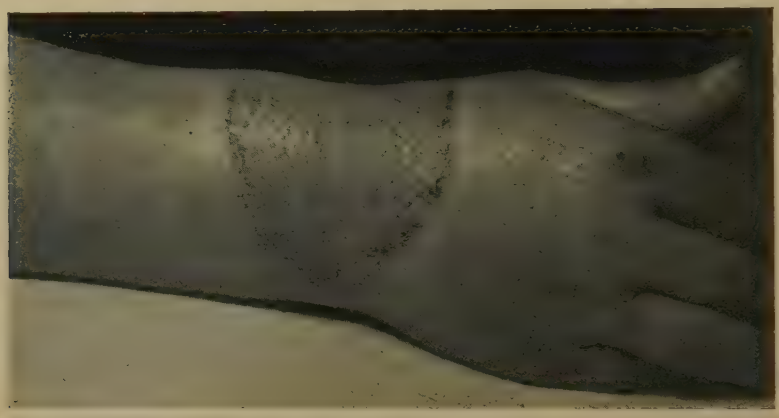

Fig. 604.—Tinea circinata.

children, and the trichophyta usually of animal origin. On the glabrous skin the eruption is seen as a scaly macule which resolves in the centre as it advances peripherally with a well-defined edge consisting of minute vesicles or pustules covered by coarse scales. Unless the organism is virulent the infection requires a week or more to show its characteristic pattern, and this helps to distinguish the disease from circinate impetigo which runs a more rapid course. The lesions usually respond to thorough inunction with Whitfield's ointment or ammoniated mercury ointment and it is often advantageous to use the ointment at night and to wash it off by day and then to apply calamine lotion containing 0·1 per cent. of mercuric chloride. Vigorous treatment often sets up troublesome dermatitis or eczema.

Tinea capitis.—In this country ringworm of the scalp in children is practically always due to microsporon infection. Typical cases show well-defined circular patches of brownish scaling and short, broken hairs. The edges of such lesions may be more conspicuous than the centres and leave no doubt as to the diagnosis. In other cases the infection is diffuse

and may closely resemble dandruff, but inspection with a powerful source of light and a Wood's glass filter reveals a greenish fluorescence in the affected hairs. The appearance is so characteristic that a single infected hair may be recognized with ease.

The diagnosis may be confirmed by finding broken hairs, and if some of the coarse scales are plucked away with epilation forceps they often carry with them short, opaque stumps. On examination in ten per cent. caustic soda solution and the high dry power of the microscope, masses of minute spores are seen to surround the hairs which have frayed ends resembling rotten rope. Exceptionally the lesions become pustular and form boggy swellings exuding pus. These pustular lesions are called

FIG. 605.—TINEA CAPITIS (MICROSPORON AUDOUINII).
The common small spored ringworm in this country.

"kerion," and although painless are often treated as carbuncles. The pustular reaction tends to destroy the fungus, so that hot fomentations of 1 in 1,000 perchloride of mercury alternating with a paint of malachite green or gentian violet will usually cure the disease in six to eight weeks.

The scaly variety of tinea capitis has to be distinguished from psoriasis, seborrhœic dermatitis and from alopecia areata, but in the absence of scurf the clean, smooth, bald areas of the latter disease present no difficulty and "note-of-exclamation" hairs are pathognomic. Patches of broken hairs occur in trichotillomania and sometimes in trichorrhexis nodosa and monilethrix (see p. 1871).

TREATMENT.—Owing to the presence of fungus and spores deeply in the follicles, it is the accepted practice to remove the hair temporarily, and two methods are employed.

(1) *X-ray epilation.*—Sub-erythema epilating doses of X-rays (350

to 400r measured with back-scatter) are given to five areas of the scalp by an expert in the technique and two to three weeks later the hair falls out, assisted manually when necessary, to obtain a total defluvium. With modern methods of measurement of the dosage, reliable apparatus and careful technique, the risk of permanent baldness is negligible, and with sedatives or using a restrictive appliance the youngest child may be treated.

(2) *Thallium epilation.*—In this method a dose of thallium acetate, accurately estimated at 8 mgm. for each kgm. of naked body-weight, is given entire in a single draught of sweetened water. The scalp hair begins to fall somewhat earlier than after the X-ray treatment, but although the epilation may be as complete, the method is not so popular. This is partly because infection may persist more often afterwards but also because fatalities have followed errors in the calculations or in the dispensing, or in the choice of subject. Toxic effects of thallium vary from slight malaise and loss of appetite and transient joint pains to albuminuria, severe nephritis, neuritis and encephalitis, so that the drug should be reserved for healthy children and limited to the younger ones for whom the carefully calculated dose does not exceed 250 mgm. Full doses of ascorbic acid reduce the incidence of toxic reactions.

No method of epilation is a cure for ringworm but is merely a device to remove infected hairs and their mosaic of adhering spores and further to facilitate the entry of the fungicides into the follicles. Thus, whilst waiting for and assisting epilation, and more intensely afterwards, every effort should be made to destroy the fungus and its spores by rubbing in Whitfield's ointment and occasionally after shampooing, painting with tincture of iodine for a day or two.

Recently more effective ointments containing phenylmercuric nitrate or salicylanilide in penetrating bases containing long chain fatty acids and polyethylene-glycol derivatives have cured scalp ringworm without preliminary epilation and it is hoped that the latter will eventually be reserved for cases refractory to the new preparations.

Treatment must be continued until a growth of healthy hair covers the scalp and after two negative examinations with the Wood's filter the child may be pronounced cured and permitted to return to school. Hats and cushions which may be infected require attention, and thought should be given to contacts from whom the disease might have arisen or to whom it might have been passed—not forgetting domestic animals.

Other varieties of ringworm of the scalp include the large spored fungi (trichophyta) and favus : they call for similar treatment. The trichophyta may produce more inflammatory lesions than the microspora and the endothrix type results in short broken stumps called black-dot ringworm. The affected hairs do not fluoresce with Wood's filter and ultraviolet light like the hairs in microsporon cases.

Favus is more common in Ireland and abroad than in this country but it can be contracted from infected mice. A diffuse infection is often indistinguishable from the common ringworms and fluorescence under Wood's filter may be present although not of the same tint. When

favus is localized, yellow, concave excrescences called "scutula" may be seen and the infected scalp has a mousey odour.

Tinea unguium.—Ringworm rarely attacks the nails in children but trichophyton and epidermophyton infections lead to the development from the free edge backwards of an opaque, subungual hyperkeratosis. Subsequently the nail becomes discoloured, irregular, friable, and has a "reeded" appearance. An asymmetrical involvement of other nails slowly ensues. The diagnosis is confirmed by examining scrapings of the matrix in a 20 per cent. solution of caustic soda with the high power of a microscope after heating the slide for a minute.

TREATMENT is unsatisfactory, but avulsion of the nail and vigorous treatment of the matrix gives the best chance of success.

Yeast infections of the skin.—The commonest yeast to infect the skin is *Monilia albicans*, the cause of thrush. Usually, if monilia lesions are present on the buttocks or about the anus, the infant will be found to be suffering from a mouth infection. Moniliasis of the skin appears as reddish-brown, scaly areas with a fairly uniform surface when the lesions occupy moist folds of the skin. Occasionally well-marked circinate lesions, similar to tinea occur on the thighs and groins. Monilia infection also accounts for a chronic intertrigo of the digital clefts and presents red, shallow fissures with white macerated cuticle in the webs of the fingers or toes. Yeasts may attack the nails, giving rise to white opaque areas beneath the nail plate and detaching it from its matrix. On scraping, a soft cheesy material can be removed and yeast cells may be seen when examined in liquor potassæ. Apart from Monilia albicans, the other pathogenic yeasts are *Monilia pinoyi* and *Monilia candida*.

Pus-coccal Infections of the Skin

Impetigo contagiosa.—Impetigo contagiosa, which used to be regarded as a streptococcal infection, is now thought to be more commonly caused by the staphylococcus pyogenes aureus. However, there is little doubt that streptococci can give rise to all varieties of impetigo. The disease is very contagious and usually affects several children in the family, particularly if in poor circumstances. The eruption generally occurs on the face but is quite common on the hands and exposed parts of the legs. It may complicate any abrasion of the skin or breach in the skin surface occasioned by parasitic infections or by the eruption of eczema. Extension of the eruption is by auto-inoculation and therefore its distribution is usually asymmetrical unless complicating some other eruption such as eczema

FIG. 606.—IMPETIGO CONTAGIOSA (STREPTOCOCCAL IMPETIGO), SHOWING THE "STUCK-ON" CRUSTS.

or scabies which is essentially symmetrical. Impetigo contagiosa occurs in the following varieties:

(1) The common scabbed sore (fig. 606).
(2) As a bullous eruption of which pemphigus neonatorum and probably Ritter's disease are varieties.
(3) A circinate type which may imitate ringworm but runs a much more rapid course (fig. 607).
(4) A scaly type called impetigo pityroides (Sabouraud). This type resembles the scaly seborrhœides and encourages the belief that some seborrhœic lesions are mild pus-coccal infections.
(5) An ulcerative type called "ecthyma," which usually occurs in debilitated children. This is the only variety which is likely to leave scars.

Fig. 607.—Impetigo with Circinate Lesions simulating Tinea circinata.

The common scabbed type of impetigo needs no further description. Bullous lesions consisting of flat, flaccid blisters on inflamed bases are often associated with crusted sores and present no difficulty in diagnosis. The rapidly spreading bullæ of *pemphigus neonatorum* are probably due to the low resistance of the infant to a hæmolytic staphylococcus aureus and in severe cases bullæ may become confluent on large areas of the body when an early fatal issue may be predicted. Infants with pemphigus must be isolated and if further cases arise, nasal and throat swabs should be taken from nurses and doctors and all possible contacts.

Circinate impetigo usually develops from the bullous type when the blister ruptures, the centre dries up, and the edges of the blebs retain infected exudate which maintains a centrifugal extension. The lesions closely resemble those of tinea circinata but run a more rapid course and are of a deeper colour.

Impetigo pityroides presents pale scaly areas resembling seborrhœic lesions and from their poor response to local treatment it seems probable that the lesions are scaly bacterides or seborrhœides.

Ecthyma occurs in debilitated children as concave ulcerations beneath

dark blood-stained crusts. The lesions run a chronic course and leave dull red depressed spots which eventually persist as white scars.

PYODERMIA OR PUS-COCCAL DERMATITIS.—Sometimes the pus-cocci produce confluent areas of dermatitis for which the diagnosis of impetigo is inappropriate. For instance, a pyogenic or pus-coccal dermatitis may spread from a septic fissure below an ear and involve the side of the face, or become super-imposed upon weeping eczema.

Pyogenic fissures and intertrigo are seen as septic cracks in the skin or as pus-coccal dermatitis involving folds and creases such as behind the ears, at the angles of the mouth, at the alæ nasi or in the napkin area (p. 1829) and are often obstinate sequelæ of impetigo.

Treatment of impetigo and pus-coccal dermatitis.—Although the majority of cases of impetigo respond satisfactorily to local treatment alone it is good practice to consider the patient and what general measures might hasten recovery. Seborrhœic subjects are especially prone to persistent or relapsing impetigo and their resistance to infection is improved by a diet rich in protein and in protective foods with limited starch, sugar and fat. Supplementary vitamins A, C and D and a palatable iron preparation are probably valuable. These measures are essential in subjects with ulcerating lesions. The nervous, irritable child, who perpetuates and spreads the infection by scratching, usually responds well to small doses of phenobarbitone. Only rarely, when an erythematous flare surrounds the lesions of impetigo, denoting a virulent organism or poor resistance, is systemic penicillin or a sulphonamide indicated. General ultra-violet light is a good supporting measure in convalescence. The local treatment depends upon the type of lesion but certain measures of general application are useful.

(1) The lesions should be cleansed with isotonic solutions of 1 per cent. sodium bicarbonate or sodium sulphate to which solution of chloroxylenol or potassium permanganate may be added.
(2) Crusts may best be removed by the repeated application of hot saline compresses. The old starch poultice may be useful at times but it is more troublesome and messy. Flat crusts on dry resolving lesions need not be disturbed.
(3) Bullæ should be snipped away with sterile scissors and the inflamed base carefully cleaned.
(4) The formation of hard crusts on the scalp can be prevented by the application of dilute mercuric nitrate ointment at night followed in the morning by saline compresses and cleansing, as described.

After cleansing, all moist lesions may be treated with proflavine 0·1 per cent. in water ; mercuric chloride 1 in 1,000 in either water or calamine lotion. When lesions become dry and crack, the yellow oxide of mercury paste is useful, especially for flexural lesions and as a comfortable application to ecthyma after removal of the crusts. Solutions of the dyes, of silver nitrate, l'eau d'Alibour (zinc sulphate 6 grains, copper sulphate 4 grains, camphor water to 1 ounce) have their advocates. The sulphonamides and penicillin should not be used locally since they are apt to sensitize the skin and lead to eczema or light sensitivity. Aureomycin 1 per cent.

or chloramphenicol 3 per cent. in emulsifying ointment may be quickly effective.

Dusting powders containing boric acid, calomel, bismuth subgallate or the organic mercurial antiseptics dry the skin and prevent auto-infection.

Pemphigus neonatorum will respond rapidly as a rule to bathing in 1 per cent. sodium sulphate and 1 in 2,000 mercuric chloride and a drying treatment, as above outlined. Greases are better avoided in this and in all other moist varieties of pus-coccal infection. If local measures fail to control a pyogenic infection the systemic use of a potent antibiotic is urgently indicated. Bacteriological identification of the causative organism should be made in anticipation of the need.

Bockhart's impetigo is a staphylococcal infection of the superficial part of the hair follicles. It is often the result of treating hairy skin with irritating mercurial or sulphur ointments especially in seborrhœic

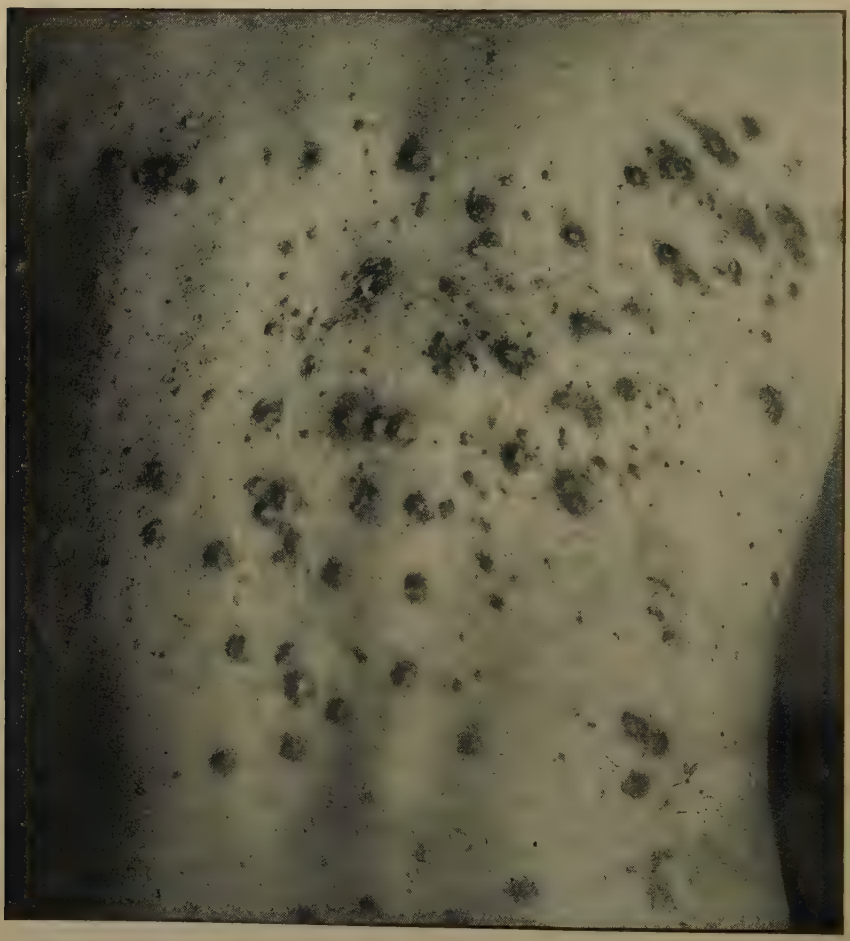

Fig. 608.—Impetigo of Bockhart (Staphylococcal Impetigo), showing Follicular Pustules.

subjects. The lesions appear as small follicular papulo-pustules with central hairs.

Treatment consists of bathing with alkaline lotion and carbolic soap and the subsequent application of a drying antiseptic lotion or paint. Mercurial preparations and solutions of proflavine or the dyes are suitable.

Furunculosis.—Boils result from staphylococcal infection involving the whole follicle, and as in the case of adults, some infants and children suffer from recurrent furunculosis. The seborrhœic subject is particularly susceptible and the general measures suggested (p. 1838) should be used to increase resistance to the infection. Alkaline baths and the application of a drying antiseptic lotion such as: phenol 10 grains, industrial methylated spirit 240 minims, solution of mercuric chloride to one ounce, to the lesions and surrounding skin prevents auto-infection.

Multiple subcutaneous abscesses in infants is a rare disease probably due to staphylococcal infection and manifest by multiple soft swellings in the skin which may be almost unaltered over them but is usually a dull red or purple. The trunk and buttocks are the usual sites affected. Scalp lesions are usually secondary to impetigo or infected eczema. Unlike boils, the abscesses are not painful. Staphylococci may be found in early lesions but the pus in older abscesses is often sterile.

TREATMENT consists of incision and drainage. The cavity may be dressed with penicillin or sulphathiazole powder.

Gangrene of the skin.—Debilitated infants and children may develop sloughing ulcers after infection with the more virulent pus-cocci, bacillus pyocyaneus, or diphtheria bacillus. Dermatitis gangrenosa also occurs as a complication of measles, vaccinia, varicella, zoster, variola and scarlet fever. Cancrum oris and noma are the terms applied to gangrenous ulcers affecting the mouth or genitals.

TREATMENT is based on the general and local measures already described.

Dermatitis vegetans is a rare type of pyogenic dermatitis in which warty granulations exuding a purulent exudate arise on the infected area. Somewhat similar vegetations are more common as a bromide eruption and may occur after iodides. These drug eruptions are usually dry. Similar vegetations occur rarely in epidermolysis bullosa.

Pyogenic granulomata. This term properly includes three types of lesion:—

(1) Ecthyma and any chronic pus-coccal ulcer.
(2) Dermatitis vegetans.
(3) Granuloma pyogenicum, a nodular type.

The last type arises after the infection of a small breach in the skin surface which leads to the formation of very vascular granulation tissue. This appears as a bright red papule which may remain dome shaped or develop into a pedunculated nodule or tumour and attain the size and appearance of a bright red cherry. The epithelium covering the lesions may be smooth and intact or the surface may be moist

or crusted. The nodule bleeds profusely after slight injury and is often mistaken for an hæmangioma. It is very persistent and will recur unless effectively curetted and its base cauterized.

Erysipelas is an acute superficial streptococcal lymphangitis of the skin. Although uncommon in the first decade, it may develop from impetigo or from an infected wound. It is manifest as a well-defined, slightly elevated, and extending erythema with flat vesicles or blebs on its surface. The constitutional signs of an acute systematic infection are present. Recurrent attacks of erysipelas are not uncommon and sometimes the same site is each time involved. When the recurrences are limited to erythema and moderate œdema of the pre-affected area, unaccompanied by fever, the condition is termed *erysipelatoid*.

FIG. 609.—GRANULOMA PYOGENICUM. A BRIGHT RED VASCULAR NODULE.

Erysipeloid (Rosenbach) resembles erysipelas but runs a slower course without constitutional symptoms, and the colour is mostly confined to the advancing edge. The eruption spreads from a small wound, usually the prick of a pork or fish bone, and is caused by the bacillus of swine erysipelas.

TREATMENT is with penicillin or sulphonamides.

Tuberculosis of the Skin

Skin lesions in tuberculosis may result from an infection with Koch's bacillus, either from without or from within. Allergic lesions, in which the presence of bacilli cannot be demonstrated, also occur in response to the specific toxins. Infection of the skin may occur through a breach in the skin surface and result in a primary lesion which is either a small ulcer or a nodule of lupus. The corresponding lymphatic gland is soon involved as in primary syphilis. More often infection of the skin is secondary to tuberculous adenitis or multiple lesions arise through a bacteræmia, the result of the breakdown of an intimal tubercle.

Scrofulodermia is the name given to a necrotic or ulcerative lesion of the skin which has become involved from a subjacent focus in a gland, bone, or abscess. The neck, face, and groins are the usual sites for scrofulodermia which resembles a chronic pus-coccal granuloma, but the granulations are eventually more exuberant and are apt to leave bridging bands of scar tissue or keloid. Ulceration is common, and the irregular, purple friable edges of the ulcers are undermined.

Treatment.—If the lesions do not respond to general measures and calciferol they may be curetted, painted with phenol and treated with small doses (150r) of X-rays, the total dose not exceeding 600r. Surgical treatment may be followed by lupus in the scar and it is of doubtful value to remove a stimulus to specific immunity.

Lupus vulgaris is a nodular variety of tuberculosis of the skin characterized by a well-defined brownish-red, somewhat translucent infiltration which on compression with glass reveals the so-called "apple jelly" nodule. Extension is slow as a rule and after months or years leads to large confluent areas or circinate lesions in or about which the characteristic nodules may usually be found. The central part of the face, the sides of the cheeks and the neck are the most common sites affected, but the limbs, buttocks or trunk may also be involved. The lesions may persist unchanged for many years and thus be mistaken for vascular nævi. On the other hand, the nodules may break down and ulcerate and if neglected lead to extreme destruction of the nose and face, leading to ectropion. The mucous membranes of the nose, mouth, and conjunctiva may be involved before or after the skin, and present red, hypertrophic granulations or active ulceration. Rarely in children, dry, warty lesions occur on the buttocks or on the extremities (lupus verrucosus). After an acute infection or exanthem in a tuberculous child a disseminated miliary lupus may appear. Many of the lesions may resolve, whilst a few persist as chronic lupus and run the usual course. The sudden clearing of lupus sometimes heralds the onset of acute pulmonary tuberculosis or meningitis.

Fig. 610.—Scrofulodermia.

The lesion on the cheek was the result of infection of the skin from a tuberculous abscess of the lachrymal sac; that on the hand was secondary to tuberculosis of the metacarpal bone.

Treatment.—The first essential is a careful general examination of the child to exclude visceral or glandular tuberculosis. Calciferol in massive doses (25,000 to 100,000 units daily) for two months, with intervals between courses, may effectively replace actinotherapy and obviate any local treatment. Otherwise intensive local and general ultra-violet light therapy are indicated if active pulmonary disease is absent. If the latter is overlooked general actinotherapy or calciferol may provoke a fatal exacerbation. Fresh air, exercise, and a diet rich in protein and protective substances are, of course, essential.

Local treatment is necessary with resistant lesions. Intensive actinotherapy with a Finsen, Lomholt, or Kromayer lamp gives the best cosmetic result but the nodules may be destroyed by painting with

Fig. 611.—Lupus Vulgaris : A Patch of Twelve Months' Duration made up of about a Dozen Lupus Nodules.
The nodules are beginning to break through the epidermis and to form crusts.

Fig. 612.—Papulo-necrotic Tuberculides.
Note central necrosis of large purplish nodule and pitted scars of older lesions.

the acid solution of mercuric nitrate, phenol, or trichloracetic acid. Lupus has been successfully excised, but recurrences may occur in scars and skin grafts and long observation should precede excision.

The tuberculides are usually regarded as allergic reactions to scanty or attenuated tubercle bacilli or to their toxins, for the organisms can rarely be demonstrated in these lesions. The most characteristic lesions are called the papulo-necrotic tuberculides, and being rare in children, will only be tabulated. Follicular papules may be superficial and are called follicular lupus or lupus miliaris disseminatus, or deep when they are termed acne scrofulosorum, acne agminata, and the facial type, acnitis. The group name, papulo-necrotic tuberculides, is often applied to the small dusky-red necrotic papules which erupt on the extremities, and in older subjects the deeper, larger subcutaneous nodules are called "erythema induratum" of Bazin. The latter commonly affect the lower part of the legs and form indolent necrotic ulcers.

The following three allergic eruptions are not necessarily specific to tuberculosis but occur in other infections, and the second type may arise as a drug eruption.

(1) *Lichen scrofulosorum* appears as groups of prominent follicles which may be pale or reddish brown and the apices are often capped with scales or horny plugs.
(2) *Erythema nodosum* (nodal fever) presents symmetrical tender red nodes on the legs and arms. It is an acute eruption often associated with moderate fever and sometimes with joint pains and is more fully described on page 801.
(3) *Lupus erythematosus* is rare in children and develops as fixed, scaly erythematous patches, usually on the central part of the face and occasionally on the neck, scalp and fingers. Horny plugs in sebaceous follicles and the opaque red surface differentiates the lesions from lupus vulgaris. The lesions do not ulcerate but progress slowly to leave smooth atrophic areas.

Virus Diseases of the Skin

Although the fundamental nature of viruses has not been determined, most of them have minute forms (elementary bodies) and exhibit many of the characteristics of bacteria, *e.g.* multiplication, adaptability, preservation of identity, specific antigenic properties, and sensitivity to antiseptics. Their essential association with living cells differentiates the viruses from bacteria and renders their study more difficult, and their smallness puts some viruses beyond the optical limits of the ordinary microscope and accounts for their filterability. However, many viruses present larger forms (the inclusion bodies), which occupy the nucleus, the cytoplasm or both, of certain cells for which the virus has an affinity. The invaded cells may carry the virus in a dormant state and, when it becomes active, toxic or degenerative changes may result in the cell or stimulation of the nucleus may lead to proliferation. Hence virus lesions of the skin may be toxic and manifest as erythematous or purpuric macules as in typhus, or the urticarial papules of measles, or the vesicular lesions of herpes and varicella, or the pustules of variola. The

proliferative lesions are seen as the papules and nodules of warts, molluscum contagiosum and orf. It is possible, but not established, that the papular eruption of lichen planus, the bullous eruptions of dermatitis herpetiformis and pemphigus vulgaris, some varieties of erythema multiforme and less likely the erythro-squamous lesions of pityriasis rosea, are also due to virus infections.

Herpes simplex or **herpes febrilis** is the commonest virus infection of the skin. The eruption arises suddenly and consists of grouped vesicles on an inflamed base. The onset may be preceded by itching or burning in the skin and it is commonly associated with acute infections and specific fevers. The usual sites are about the lips and the cheeks, but it may occur on the buttocks, genitals or limbs. It is usually unilateral, but not so sharply so as zoster nor is it so accurately localized to spinal segments. The majority of infants are probably infected early in life and it is thought that gingivo-stomatitis is the primary herpetic lesion in many cases. Rarely the primary herpetic infection of weeping eczema gives rise to Kaposi's varicelliform eruption, to be described shortly. About 70 per cent. of adults carry the virus and its presence may account for the persistence of herpes-antibody in the serum and also for the tendency to relapse. This tendency may be marked in the condition called "recurrent herpes" when new outbreaks may occur at intervals as short as a month for several years. It has been shown that foci of irritation or infection may be important factors in relapsing herpes, and this should be considered in treatment. Ample proof exists that herpes febrilis is due to a virus and that rabbits and guinea-pigs can be readily infected with it. It is odd that although the presence of specific antibodies can be demonstrated in many cases, there is no solid immunity which characterizes many other virus infections.

FIG. 613.—HERPES FEBRILIS—RECURRENT HERPES: A SEVERE EXAMPLE OF FACIAL HERPES.

The boy had had several attacks. There was a temperature of 100° F. and some malaise, but there were no other symptoms.

TREATMENT of the recurrent type is unsatisfactory, but full doses of nicotinic acid may diminish the tendency of herpes to recur and X-rays (doses of 100r repeated in three weeks for three doses) sometimes stop recurrences. Two per cent. of phenol in calamine lotion is a suitable local application, and greasy preparations should be avoided.

Zoster may occur in children, although it is more common in adults. The eruption is similar to that of the herpes febrilis but affects areas

of skin corresponding to the distribution of the sensory fibres of one or more of the sensory ganglia. It is seen most characteristically affecting

FIG. 614.—RECURRENT HERPES.

unilateral zones on the chest (fig. 615), but it is not uncommon on one side of the forehead, face or neck, and may affect one arm or one leg. The virus concerned is probably a modified strain of the virus of varicella and it should be remembered that zoster patients are very apt to give varicella to young children who have not previously had the disease.

FIG. 615.—HERPES ZOSTER SHOWING ZONAL DISTRIBUTION.
Dorsal 4, 5, and 6, segments.

A generalized infection with the virus is much more likely to produce varicella and subsequently residual virus probably remains latent in certain posterior root ganglia until some alteration in the patient's resistance, which may be induced by an operation, a severe shock, or a toxic drug, permits the virus to become active. Then the symptoms of neuritis mark the descent of the virus down the sensory nerves to the skin, where the eruption develops. The virus has been shown to be present in the vesicles. In this disease a solid immunity follows an attack and a recurrence is extremely rare. The virus is not that of herpes and the ordinary experimental animals are not susceptible to it.

Treatment.—Systemic aureomycin has given promising results and doubtless some antibiotic or a pituitary hormone will become the treatment of choice. Daily injections of posterior pituitary extract up to 0·5 c.cm. or sodium iodide in doses up to 5 grains two or three times a day are thought to be beneficial, but the variability presented by zoster makes the assessment of therapeutic measures difficult. Rest in bed, the application of calamine-phenol lotion to the lesions, and sedatives to relieve symptoms are often all that is necessary, for pain is less marked in young subjects and may be absent.

The exanthemata produced by virus infections will be described elsewhere, but reference will be made here to vaccinia.

Vaccinial eruptions.—The uncomplicated vaccinial lesion closely resembles a typical lesion of smallpox arising as a vesicle on an inflamed base and proceeding to the formation of a pustule with some umbilication and then varying necrosis of the central part and ultimate resolution to a depressed scar. Auto-inoculation from the active lesion may produce disseminated vaccinia and sometimes the lesions, especially if affecting the genitalia, may be large and œdematous, suggestive of primary syphilis. In some children diminished susceptibility accounts for a generalized eruption of discrete vaccinial papulo-pustules. Vaccination may be complicated by a pus-coccal infection, which is almost inevitable unless clean lymph is used and antiseptic precautions are taken. With modern technique there is no danger of introducing tuberculosis or syphilis. Transient erythematous or urticarial rashes may occur with vaccination. Infantile eczema is nearly always aggravated by vaccination, which is therefore better deferred in these subjects and in those who have a family history of eczema or asthma.

Kaposi's varicelliform eruption is a rare disease usually affecting an eczematous infant. The eruption is more like variola than varicella and its distribution, on the face and limbs chiefly, implements the analogy. Moderate or severe pyrexia is usual and a secondary pus-coccal infection quickly produces an alarming appearance, the whole face and the limbs being thickly crusted with purulent exudate and studded with papules, vesicles and pustules. The morphology of the discrete lesions is suggestive of variola. The disease is usually due to a primary infection of the open eczematous lesions with the virus of herpes or vaccinia and a history of contact with these diseases may be obtained. The essentials of treatment are to dry the lesions and to control infection. Aureomycin is

probably the best antibiotic to use but cases have responded well to systemic penicillin and to proflavine solution locally.

FIG. 616.—KAPOSI'S VARICELLIFORM ERUPTION ON FACIAL ECZEMA.

Dermatitis herpetiformis and *pemphigus vulgaris* are regarded by some authorities as virus diseases although the supporting evidence is inconclusive. Fortunately these diseases are very rare in the first decade. The clinical features may be similar and sometimes the diagnosis

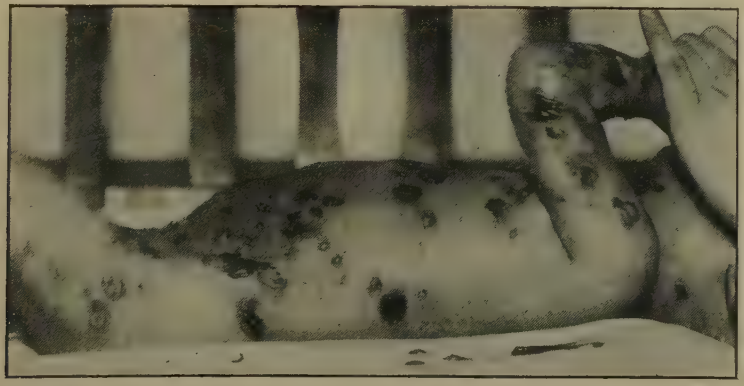

FIG. 617.—PEMPHIGUS VULGARIS IN A CHILD OF TWO YEARS OF AGE.

is uncertain until a long period of observation has elapsed. Dermatitis herpetiformis is much more likely to be the diagnosis than pemphigus vulgaris.

Dermatitis herpetiformis (Duhring's disease) presents a vesicular or bullous eruption arising upon circinate or polymorphic erythematous areas. The trunk is mostly affected but the limbs are not spared. Itching may be troublesome and scratching causes secondary infection and produces scabbed sores, residual scars, and patchy pigmentation. The disease often runs a prolonged course and may persist for ten to fifteen years with eruptive phases recurring after varying periods of quiescence. Mild cases may be mistaken for chronic eczema or impetigo.

TREATMENT is unsatisfactory but arsenic often controls an attack. Small doses of sulphapyridine given over six to eight weeks have sometimes given good results. Ascorbic acid should be given with these drugs. Local treatment is designed to dry up the vesicles and prevent infection. Watery solutions of the dyes are useful for this purpose.

FIG. 618.—VERRUCÆ VULGARIS. MULTIPLE WARTS. BOY AGED FIVE.

Pemphigus may be distinguished by the fact that many bullæ becoming pustular erupt on apparently sound skin and lesions occur in the mouth and on the eyes. The prognosis of pemphigus vulgaris is always grave. Aureomycin is occasionally an effective remedy for pemphigus and dermatitis herpetiformis. It should be remembered that bullous eruptions in infants are usually bullous impetigo (pemphigus neonatorum) or bullous urticaria, and in older children a bullous erythema multiforme is much more common than pemphigus or dermatitis herpetiformis which are rare diseases in children. The congenital disorder, epidermolysis bullosa, presents similar bullæ after slight trauma.

Verrucæ or **warts** are small growths of the epidermis provoked by the presence of a virus in the cells of the Malpighian layer. Acidophilic

bodies in the cytoplasm and basophilic ones in the nuclei of affected cells have been described as inclusion bodies. The infectivity of warts has been demonstrated and is supported by abundant clinical evidence. Warts may be solitary or numerous. They exhibit various patterns and may persist indefinitely or disappear spontaneously.

The common wart (verruca vulgaris) has plane, digitate, and filiform varieties of which the plane type is apt to be confused with a papular eruption such as lichen planus.

Plantar warts are painful and may be epidemic in boarding schools.

Treatment. The only certain cure is the complete destruction of every wart, but as this procedure is tedious, painful, and apt to leave scars, more cautious methods are usually employed. Daily painting with phenol, 50 per cent. trichloracetic acid, glacial acetic acid, or 10 per cent. of salicylic acid in flexile collodion is often successful and is more effective if the horny cap is pared before painting and the lesion kept under adhesive plaster. Solitary warts respond to efficient freezing by CO_2 snow but the method is painful. Light cauterization with the diathermy needle or galvano-cautery is often successful. X-rays and radium should only be used by experts and it is better to combine moderate dosage with other methods since the virus is probably less susceptible to irradiation than the infected cells. Thompson advised soaking the feet daily in 3 per cent. of formalin in saline for twenty to thirty minutes as a cure for plantar warts, but some cases are resistant.

Molluscum contagiosum is caused by a different virus which produces a lobulated epidermal growth having a smooth, dome-shaped, umbilicated, pearly papule or nodule. A cheesy white material may be expressed from a ripe lesion and this consists of the elementary bodies of the virus.

The lesions should be curetted and the bases cauterized, or the centres of the mollusca may be destroyed by phenol or the galvanocautery.

The condition may respond to a prolonged course of a sulphonamide.

GROUP 5.—DISEASES DUE TO COLD

Perniosis—acrocyanosis—erythema pernio—erythrocyanosis cruris puellarum—livido reticularis

Perniosis is the term given to the chilblain group of disorders. The most common manifestation is acrocyanosis, a condition in which the hands and feet are congested, blue, and cold in cold weather. The condition is more common in the debilitated, especially in tuberculous subjects. When severe, acrocyanosis is often thought to be Raynaud's disease, which fortunately is extremely rare.

Acute chilblain, erythema pernio, is especially prone to occur in subjects with acrocyanosis. The lesions develop as localized hot, red, œdematous areas, especially affecting the fingers and toes. Irritation may be severe in the early phases but the symptom disappears when

the skin surface breaks and relieves tension. The lesions are then described as broken chilblains and secondary infection usually occurs and delays healing. The diagnosis is simple.

Treatment.—Attention should be given to diet and the general health of the patient. Thyroid, nicotinic acid, vitamin K, calciferol or halibut oil are usually helpful. The limbs should be warmly clad and this is the most important factor in the prevention of chilblain. To the early lesions a lotion of phenol 10 grains, tincture of iodine 60 minims, camphor water to 1 ounce will relieve irritation, but when the skin is broken the lesions should be dressed with an iodine ointment.

Erythrocyanosis cruris is another variety of chronic perniosis which is more common after adolescence but may occur before it. The condition develops as bluish discolorations on the lower thirds of the legs. It may closely imitate Bazin's erythema induratum but is less well defined, is not appreciably indurated, and practically never ulcerates.

Livido reticularis is a blue or purple mottling of the skin usually affecting the limbs. As suggested by the name, the discoloration, which is due to stasis in the superficial venules, produces a coarse network. It usually affects ill-nourished children or those with chronic systemic diseases and its presence is an indication for careful clinical examination.

GROUP 6.—TOXIC AND DRUG ERUPTIONS

Erythema multiforme—purpura—urticaria—granuloma annulare—drug eruptions—psoriasis—pityriasis rosea—lichen planus—alopecia areata—leucodermia—exfoliative dermatitis

Toxic eruptions are usually erythematous or urticarial or a blend of the two. The first group is described as the erythemata of which the essential lesions are red macules occurring as discrete spots or large sheets. The generalized erythema which characterizes scarlet fever is typical of this group and scarlatiniform rashes occur as prodromal eruptions, or in some phases of other exanthemata. Blotchy erythematous rashes are common as toxic eruptions of alimentary origin, usually following the consumption of bad fish or tinned food, but also occurring seasonally with certain foods such as strawberries and plums. Similar eruptions may be the response to certain drugs such as the sulphonamides, arsenic, or belladonna. The toxic erythemata may be mistaken for the rashes of specific fevers, and the variety called acute scarlatiniform erythema is exactly like that of scarlet fever, but constitutional symptoms are absent and a careful history may provide a clue to the toxic origin.

Erythema multiforme is a collection of clinical types of toxic erythemata having fairly constant patterns. Although different types of lesions occur together and account for the title, often one pattern is predominant, such as varicoloured concentric rings (erythema iris), annular lesions (erythema circinata), bullous lesions (erythema bullosum),

and papular lesions (erythema papulosum). Erythematous macules of various sizes may occur alone or be mixed up with the other lesions.

As in the case of other toxic eruptions, the eruption is usually symmetrical and shows either a peripheral distribution on the limbs or central on the body, but may be universal. Erythema iris commonly occurs on the hands and forearms and tends to recur, whereas bullous lesions are more frequent on the trunk and second attacks are rare. The tongue, buccal mucosa or the genitals may be affected, and severe cases are often described as the Stevens-Johnson syndrome. Moderate fever, joint pains and gastro-intestinal disturbances point to a general toxæmia and some lesions may be purpuric. It is unlikely that erythema multiforme has a specific ætiology but a virus or streptococcal infection may account for some cases and herpes may precede the eruption.

The disease is rarely serious and the eruptions usually fade within five to ten days.

FIG. 619. ERYTHEMA MULTIFORME CIRCINATE LESIONS. GIRL AGED THREE YEARS.

TREATMENT.—The patient should be kept in bed and carefully examined for evidence of infection, and a white cell count and sedimentation tests may be of value. Salines, ascorbic acid, vitamin K and calcium are useful in mild cases. Calamine lotion serves as a local application. Penicillin or a sulphonamide is effective in severe cases of streptococcal origin, and streptomycin, aureomycin and chloromycetin have been successful in resistant cases.

Purpuric eruptions are distinguished by the fact that the bright red macules persist under pressure with a glass spatula. Like erythema multiforme, purpura may be associated with toxic arthroses or gastro-intestinal disorders, but lesions also occur as familial anomalies of the capillaries and are symptomatic of certain diseases of the blood, bone-marrow, liver and spleen (see page 1080). Purpuric lesions mark the severe phases of toxic and exanthematous eruptions.

PURPURA SIMPLEX is more common in children than in adults and the condition may be familial. The lesions consist of petechiæ and small macules and mostly appear on the lower limbs. Little or no constitutional disturbance accompanies the eruption and rest and good food are more useful than any particular vitamin.

HENOCH'S PURPURA presents a similar picture but is associated with gastro-intestinal symptoms and blood in the stools.

Purpura rheumatica, peliosis rheumatica (Schönlein's disease) is often more extensive on the limbs and is accompanied by articular pains and swellings.

These two varieties are sometimes termed *anaphylactoid* purpura for no particular reason, and pyrexia and some constitutional disturbance are usual.

Urticaria.—The essential lesion of urticaria is the wheal which is the major manifestation of the skin to histamine in the triple response of Lewis (see page 1815). The provocative injury may be trauma, stings of nettles, insects, or jelly-fish, or exposure to heat or cold. Generalized urticaria is due to the same mechanism brought about through offending allergens or toxins such as foods (shellfish, eggs, mushrooms, strawberries), drugs (aspirin, sulphonamides), sera, and bacterial toxins from focal sepsis. Some types of urticaria are erythematous, especially those which develop after enemata or injections of serum.

The papular urticaria of young children presents a different clinical picture and runs a chronic course. It has been described on page 1839.

Treatment.—The provocative agent, food or drug, should be avoided, and alkaline aperients and small doses of grey powder assist elimination. It is probably useful to give extra calcium and vitamins D and C, and a sedative if symptoms are distressing. Sometimes small doses of ephedrine hydrochloride give rapid relief. Antihistamine drugs are inevitably prescribed and vitamin K may be of value when they fail. Two per cent. of phenol in calamine lotion is a suitable local application.

Granuloma annulare is presumably a toxic eruption and consists of annular lesions suggestive of tinea on first sight, but the margin is composed of firm, white, or pink nodules or a continuous ring which has the appearance of cartilage in the skin (fig. 620). Lesions most commonly appear about the knuckles and joints of the fingers, but also affect the wrists, forearms, and legs and rarely the body. The eruption may persist for months or years without symptoms and eventually resolve without scarring. The cause of the eruption is unknown, but certain chronic annular erythemata occurring in adults present very similar features and all are probably allergic phenomena. Subcutaneous nodules similar to rheumatic nodules have been observed and the histology lies between that of the latter and early tuberculosis.

Treatment.—Patients should be carefully examined for evidence of latent tuberculosis or other infections, and the lesions may be treated with small doses of X-rays or kept occluded by adhesive plaster. ACTH appears to cause a remission.

Drug eruptions.—Children may react to many drugs, as in the case of adults, and there is no space to give a comprehensive list here. Whenever a sudden and unaccountable eruption appears, especially if the colour tones and morphology of the lesions are somewhat unusual, the question of drug origin should be carefully considered. Phenobarbitone may produce a fine papular eruption simulating german measles. The sulphonamides and belladonna usually produce patchy or generalized erythematous eruptions. Iodides may give rise to acneiform,

FIG. 620.—GRANULOMA ANNULARE.

FIG. 621.—BROMIDE GRANULOMATA.

vesicular, bullous, or pustular lesions which may imitate varicella or variola. Bromides sometimes produce curious warty pink granulations which may be mistaken for a neoplasm (fig. 621). Phenolphthalein accounts for odd purplish ringed-lesions of erythema multiforme type; in some cases the eruptions are fixed, *i.e.* they recur on the same sites whenever the drug is retaken. Phenazone and other drugs have caused "fixed" eruptions.

FIG. 622.—PSORIASIS.

Psoriasis.—Psoriasis is not uncommon in children. In about 40 per cent. of cases there is a familial history. Psoriasis may be acute or chronic. Sometimes in children an acute eruption of small, scaly pink lesions appears on the trunk with fewer lesions on the limbs. The child may have slight malaise and if put to bed and treated with salicin or salicylates may recover completely in three or four weeks and have no further trouble. More often the disease is chronic and affects the limbs, especially the extensor aspects where the characteristic pink lesions with a silvery scale are found upon the elbows and knees. In severe cases much of the body is also involved and the lesions may be small, scaly spots or large areas. Sometimes circinate lesions suggestive of tinea may be predominant and this variety is usually more obstinate to treatment.

Psoriasis in the scalp is characterized by discrete, thickly crusted, rocky-hard nodules which may be distinguished from pityriasis capitis by palpation alone. The nails may show thimble-like depressions and subungual hyperkeratosis. Rarely pustular lesions develop and are often limited to the palms, soles, and digits. The pustules are sterile and may thus be differentiated from ringworm infections or chronic pus-coccal lesions. This type is also very resistant to therapy and responds best to the removal of some focus of infection, especially in the tonsils.

DIAGNOSIS.—In a typical case the silvery appearance of the scales at once suggests psoriasis, but in recent cases the patches may be red and smooth, and only show scales on scraping with the nail or a blunt instrument. It is characteristic of the lesions of psoriasis—(1) that the sharply-circumscribed patches grow by extension at their margin, not by

coalescence of smaller patches; (2) that they always remain dry; (3) that on scraping the scales become more obvious, until at length a level is reached where there are no more scales, but a dry, red, smooth surface, which shows bleeding-points on further scraping; (4) that the red patch which remains after the scales have been removed shows no infiltration, and fades on firm pressure—*i.e.* the lesion is a scaly macule, not a papule.

The cause of psoriasis remains obscure, but it appears likely that it is an allergic reaction of the skin to some toxin with a primary metabolic factor that is not understood.

TREATMENT should therefore include the consideration of these

FIG. 623.—PSORIASIS. CIRCINATE OR FIGURATE TYPE.

probable ætiological factors, and it is inadvisable to use toxic drugs such as arsenic. A well-balanced diet with restriction of starch and fat and adequate protective foods, augmented if desired by vitamin concentrates, especially B, C and D. General ultra-violet light is often a most valuable measure and it should be given in the fullest doses tolerated. An inunction of coal tar ointment at night, cleaning with a simple oil next morning and general irradiation followed by hot baths often give good results. For routine use an ointment of :—

℞ Solution of coal tar . . 30 minims.
Salicylic acid . . . 10 grains.
Ammoniated mercury ointment to 1 ounce.

is indicated and dithranol ointment B.P. should be reserved for localized obstinate lesions. Strong applications should never be employed when psoriasis is widely spread or when the lesions are brightly coloured because an exfoliative dermatitis may result. A useful bland application is 5 per cent. of ointment of mercuric oleate in ichthyol cream.

Pityriasis rosea is not uncommon in children but usually causes difficulty in diagnosis. The first lesion, called the herald spot, is a round or oval scaly rose-pink patch on the trunk or adjacent part of the limbs. In a few days the central part of the lesion pales and the edges extend producing a circinate pattern closely resembling tinea circinata. After five to ten days a dramatic extension of the eruption occurs on the trunk where the oval lesions, still somewhat similar to the "herald patch," often have their long axes in line with the ribs. The body lesions have pale centres surrounded by a collarette of elevated marginal scales, which may be a marked feature. The eruption usually lasts six to eight weeks and then disappears, leaving no permanent mark. Itching is less marked in children than in adults and may be absent. Although the clinical course suggests some infection of the skin with a primary spot, an incubation period and a secondary eruption, no organism has been found and the ætiology is obscure.

Apart from tinea, the eruption has to be distinguished from psoriasis and seborrhœic dermatitis, particularly the circinate type.

Treatment is on general lines, and a suitable local application is 2 per cent. each of phenol and precipitated sulphur in calamine lotion. Ascorbic acid and small doses of quinine, salicin or grey powder may be given.

Lichen planus is rarely seen in children, but the eruption is readily recognized as flat-topped, lilac tinted, burnished papules, having fine white striæ on their surface. The lesions often affect the flexural aspects of the forearms and usually itch, but this symptom is less marked in children than in adults. Occasionally hypertrophic or warty lesions are seen on the extremities and are extremely persistent.

The cause of lichen planus is unknown and therefore it is justifiable to include it in this group of eruptions due to toxic factors, but some hold the view that lichen planus is a virus infection, for which there is no definite evidence.

The disease is little affected by treatment. Aneurine in full doses, a sedative to relieve itching, and a lotion of phenol 2 parts, glycerine 6 parts and solution of mercuric chloride to 100 parts are usually adequate.

Alopecia in children.—Reference has already been made to congenital alopecia arising as an ectodermal defect. After excluding this variety one is left with the functional disturbance called alopecia areata and the various scarring alopecias that result from some previous injury or inflammation of the skin such as burns, pus-coccal infection, favus, and some of the pustular ringworms and from an overdose of X-rays. Syphilis, pseudo-pelade and lupus erythematosus are also rare causes of cicatrical alopecia.

Alopecia areata may be diffuse or localized. A mild falling of the hair occurs after severe illnesses, in severe anæmia, and in hypothyroidism.

The ordinary type of alopecia areata develops quickly as smooth, clean, bald areas on the scalp. In the edges " note of exclamation " hairs may be seen and sometimes thin white hairs. Both clearly denote a diminished activity of the hair papillæ and indicate the functional origin of the disease. The subjects are frequently nervous children, and a history of some shock or fright is so common that there can be no doubt that the activity of groups of hair follicles is suspended through the action of the vegetative nervous system influenced by the endocrine glands. Severe toxæmia may also operate the same mechanism and sometimes, when a child contracts one fever after another, such as measles, chickenpox,

FIG. 624.—ALOPECIA AREATA.

or mumps, every hair on the scalp, eyebrows and eyelids may fall (alopecia totalis).

The diagnosis of alopecia areata is easy if care is taken to exclude the atrophic conditions previously described.

The clean bald areas with " note of exclamation mark " hair-stumps in the boundaries are characteristic. *Ringworm* of the scalp in children is almost invariably of the small-spored type and the lesions are scaly, often discoloured and the baldness is only partial because the infected hairs break away in fragments like frayed and rotten rope (see fig. 625). Two other conditions account for undue fragility of the hair and may simulate alopecia or tinea. *Monilethrix* is usually seen in children who may have had an apparently normal head of hair at birth but a few months later a diffuse and maybe total alopecia occurs to be followed by a regrowth of hair which breaks off before attaining any length. On examination under the microscope the affected hairs are seen to have alternate nodes of normal width alternating with marked and uniform constrictions giving a beaded appearance. Little can be done

to affect the condition which appears to depend upon a dystrophic lesion of the hair follicles and familial cases are common. Monilethrix tends to disappear about the age of puberty. *Trichorrhexis nodosa* is more common in adults and may be regarded as an acquired fragility of the hair shaft due to excessive washing or bleaching of the hair. Slight trauma to the affected hairs gives rise to nodal swellings due to focal, longitudinal splittings of the hair fibrils giving the appearance of two brushes stubbed together. Fracture occurs readily at these nodes.

Treatment of alopecia. The essential treatment is that of a nervous child with varying degrees of debility and possible focal infection. General tonics and extra vitamin B complex in the form of yeast are indicated and little should be expected of local therapy. Any method of counter

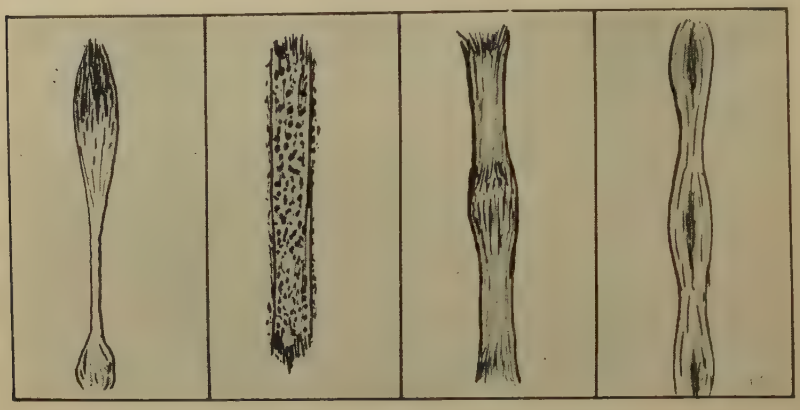

FIG. 625.—DIAGRAM OF HAIRS.

1. Alopecia areata. "Note of exclamation" hair.
2. Small spored ringworm of hair.
3. Trichorrhexis nodosa.
4. Monilethrix.

irritation such as a cantharides lotion, erythema doses of ultra-violet light or massage will, of course, improve the blood supply to the whole scalp, but it will not affect those follicles which are inhibited by the sympathetic nervous system.

The prognosis is usually good but it is difficult to predict how soon the hair will return. Cases of total alopecia respond even more slowly. The first hair to return is usually fine and white, but soon thickens and becomes pigmented. Cortisone and ACTH have been used with only temporary, or without, success in the treatment of alopecia totalis.

Leucodermia (**vitiligo**) is a mysterious depigmentation of the skin in patches which is not infrequently associated with alopecia areata and may depend upon a similar mechanism. If the scalp is affected patches of white hair result and may be taken for a resolving alopecia areata or for a congenital white tuft. Leucodermia is often noticed for the first time after exposure to sunlight when the unaffected areas of skin show

hyperpigmentation, which contrasts sharply with the depigmented areas of otherwise unaltered skin affected by the disease. There is nothing in the histopathology, or to be obtained from a general examination, to indicate the cause of the affection.

TREATMENT.—No local treatment appears to be of value, but the white areas may be tinted with permanganate solution or walnut stain to obscure the blemishes.

FIG. 626.—VITILIGO, OR LEUCODERMA.

The white areas are the result of loss of pigment. The rest of the skin is normally pigmented.

Generalized exfoliative dermatitis (dermatitis exfoliativa, pityriasis rubra).—This rare condition is not a specific entity and it is characterized by a universal erythema with varying degrees of

FIG. 627.—KELOIDS, FOLLOWING BURNS FROM BOILING WATER.

œdema of the skin and followed by extensive desquamation so that handfulls of scales may be shed. Itching is often severe.

The mild toxic variety has already been described under the term scarlatiniform erythema, but more severe forms may arise as a primary idiopathic eruption or secondary to eczema, seborrhœic dermatitis, psoriasis, or to treatment with a toxic drug such as arsenic, bismuth, gold, or a sulphonamide.

The types of exfoliative dermatitis affecting infants are usually of pyogenic, seborrhœic or psoriatic origin and the first and second have

already been described and associated with the names of Ritter and Leiner.

Treatment.—The patient should be investigated in an attempt to find a specific cause and then treated symptomatically. Compresses of glycerine and lead lotion or emollient creams are the most suitable applications, and a paint of 0·5 per cent. gentian violet in water is useful and prevents secondary infection.

Keloids are hypertrophic scars and they have already been mentioned as sequelæ to scrofuloderma. They may arise unaccountably after burns (fig. 627), vaccination, or upon the scars of wounds or operations. Treatment with radium or X-rays is often successful, but they should not be excised unless the excision is shortly followed by prophylactic X-ray therapy.

CHAPTER XXXVII

MALIGNANT DISEASE IN CHILDREN

ALAN SMALL

It is a melancholy fact that the morbidity and the mortality of malignant disease approximate closely. Since cancer in children is no exception it is fortunate that the disease is uncommon. But although uncommon it is not so rare as to be clinically unimportant, and indeed it ranks high among the killing diseases of secondary importance. The mortality as compared with that from some commoner diseases is shown in the table.

TOTAL DEATHS (UNDER 15) FROM CERTAIN CAUSES, ENGLAND AND WALES

	1942	1947
Cerebrospinal fever	690	371
Congenital pyloric stenosis	359	336
Cancer and tumours	410	483
Scarlet fever	78	33
Osteomyelitis	156	27
Leukæmia	209	273
Syphilis	134	89
Road traffic accidents	1087	824

Note.—The diseases included in this table have been arbitrarily chosen as common diseases causing approximately the same number of deaths in this age period as cancer and tumours.

It is probable that the actual incidence and death-rate is higher than that shown in the table because imperfect certification is particularly likely in children. Many cases are recorded under indefinite headings and under secondary effects in individual organs. The figures for Greater London are considerably higher than those for the country as a whole and this is probably due to a more thorough pursuit of the ultimate cause of death in the hospitals in that area. It may be noted that the increase between 1942 and 1947 is 18 per cent. under the heading cancer and tumours and 30 per cent. under the heading leukæmia. This is probably due to more accurate diagnosis and not to any real increase.

It is proposed to discuss in this chapter certain general features of malignant disease in children, followed by an account of the principal varieties.

General considerations.—Malignant disease at any age is a disorder of growth the causes of which are as hard to find as the springs of life itself. As a simplification they may be divided into two groups—internal and external. The internal group includes inborn factors—often confined to one area or organ—as well as those affecting the organism as a whole and probably related to hormonal effects. Cancer in children results almost entirely from inborn factors. It is impossible to do more than suggest that inborn errors of tissue and organ growth may result in early malignant disease. In children malignant disease is an aberrant growth rather than a true new growth. The disease most commonly manifests itself

within the first five years of life and indeed it may frequently begin before birth. It occurs less frequently in the second five years and less frequently still in the third five-year period. As age increases the inborn defects of growth manifest themselves less commonly, having, in the majority of cases, declared themselves early if present at all. In this same age group the factors contributing to cancer in the adult have not exerted their influence. Except for a few intracranial tumours and an occasional osteogenic sarcoma, malignant disease is extremely uncommon at the end of the childhood period. Extrinsic factors of chronic irritation and others less well known are slow to act and, with the exception of ultra-violet light in xeroderma pigmentosum, are largely unimportant in the production of cancer in children. Although this is generally true, a few remarkable exceptions occur to indicate that knowledge of the causes of malignant disease is far from complete. Thus cancer of the buccal mucosa—a growth occurring typically in old people with a long history of chronic irritation—has been recorded in a child of four months. The literature abounds with similar examples of curiosities.

Malignant disease in children is largely confined to a few conspicuous entities. Carcinoma (squamous or adenocarcinoma) is rare and the great majority of growths are sarcomatous or embryonal in origin. The commonest group, that of malignant tumours of the central nervous system including the retina, has been fully described elsewhere (p. 1259) and the leukæmias, which fulfil all the criteria of malignant disease, are dealt with under diseases of the blood (p. 1091). Modern views on lymphatic tissue and the histogenesis of its tumours make a most intimate relationship between leukæmia, lymphosarcoma and Hodgkin's disease reasonably certain. For the present these are described separately as clinical entities, though there is now little pathological support for this distinction. Closely following tumours of the central nervous system in numbers are tumours of the sympathetic nervous system and embryoma of the kidney which account between them for half the remainder.

Congenital tumours

A few cases of transmission of malignant tumours from mother to fœtus have been recorded but they are so rare as to be pathological curiosities rather than a clinical problem. This transmission has been proven in malignant melanoma and lymphosarcoma. It is strange that it has not apparently been recorded in leukæmia nor has transmission from fœtus to mother (a theoretical possibility in neuroblastoma and others).

As a living organism the child is already nine months old at birth. Attention has already been drawn to the importance of inborn factors in carcinogenesis in children and as these are present from conception it is not surprising that malignant tumours are occasionally present at birth. The literature provides many examples of such tumours representing every common variety. Moreover many tumours recognizable only after they have reached a large size during the first year or two of life probably have an intra-uterine genesis. This has no particular clinical

significance except to illustrate the absence of external factors in this genesis and the danger of excluding malignancy from the diagnosis at any age. The commonest congenital malignant tumours are retinal gliomata, neuroblastomata, embryomata of the kidney, soft tissue sarcomata and hepatomata. Hereditary influences have not been traced in any of these with the exception of retinal glioma.

Neuroblastoma.—This, with intracranial tumours, is the commonest malignant disease in children, and is virtually beyond treatment. Its origin is from the primitive cells of the sympathetic nervous system and it may therefore arise wherever these develop. By far the most common site

FIG. 628.—NEUROBLASTOMA.

of origin (two-thirds) is the adrenal medulla and the remaining third are distributed among the abdominal, thoracic, pelvic and cervical ganglia in that order of frequency. The tumour is one of the earliest years, occurring in a series of sixty-two consecutive sufferers as follows :

0–1 (12) 1–2 (12) 2–3 (11) 3–4 (13) 4–5 (2) over 5 (12).

Its onset is particularly insidious and it has been known to develop under the very eyes of the pædiatrician. The commonest presenting symptom is " enlargement of the abdomen " with the finding of a tumour mass on examination. As a rule this recognition of a tumour calls attention to preceding and possibly disregarded symptoms—pallor, weakness, loss of weight or failure to gain, anorexia or vomiting. In 10 per cent. or more of cases, the first sign is a precocious metastasis—most commonly in the orbital region or liver, less commonly elsewhere in the skull or in cervical

lymph nodes. These precocious metastases may occur in any bone and may be confused with other neoplasms of bone (see fig. 645) (see also the section on Ewing's tumour). In some cases though preceded by other

FIG. 629.—NEUROBLASTOMA (HUTCHISON'S SYNDROME).

symptoms a metastasis is recognizable on clinical examination without the finding of a primary tumour. The radiological appearance of these metastases is largely one of bone destruction, but there is often a curious

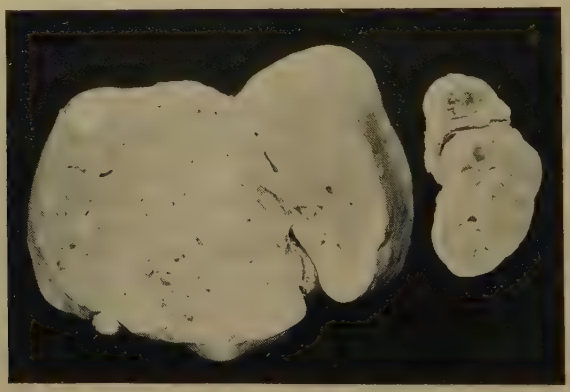

FIG. 630.—NEUROBLASTOMA (PEPPER SYNDROME).

spiculation which may resemble the appearance of osteogenic sarcoma (fig. 646). Another common presenting symptom (10 to 15 per cent.) is pain in the back or legs associated with or followed by weakness in the legs, due to invasion of the spinal canal by direct extension or by osseous metastases. Occasionally a direct extension of the primary tumour

presents in an unusual situation —lumbar, sacral or chest wall (fig. 631). In the pelvis, interference with micturition may be a prominent early symptom, and thoracic primary growths may present with signs of tracheal irritation or obstruction. The frequent occurrence of metastatic presentation is an indication of the phenomenal malignancy of the disease and when such a metastasis is recognized either as a presenting sign or on routine investigation (which should include skeletal X-ray examination) the patient is beyond treatment. The constant and severe anæmia associated with neuroblastoma is of obscure origin since it may be unaccompanied by osseous metastases and may occur without any apparent blood loss. An upper abdominal mass accompanied by anæmia is more likely to be of sympathetic than of renal origin. The differential diagnosis is from embryoma of the kidney, splenic enlargement, hepatic tumour, leukæmia, scurvy and, though less likely to confuse, from other renal swellings and intra-abdominal masses. A neuroblastoma of adrenal or retroperitoneal origin may cause distortion or obliteration of a pyelogram by compression or invasion of the kidney. As operation is the only treatment for both, laparotomy should be performed without waste of time in all doubtful cases. The neuroblastoma is, as a rule, rather more fixed on clinical examination, tends to cross the midline and may, of course, be associated with osseous, hepatic or glandular metastases. This fixation is associated with peritoneal and retroperitoneal adherence which, together with the discoloured appearance of the tumour on laparotomy, may enable the operator to make a correct diagnosis with some confidence. If the tumour is a neuroblastoma removal is seldom possible, but if practicable it should be undertaken since a few cures have been reported.

FIG. 631.—MALE, AGED ONE YEAR. NEUROBLASTOMA. LUMBAR PRESENTATION WITH PARAPLEGIA.

It has already been said that the disease is almost beyond treatment. Nevertheless some remarkable spontaneous recoveries have been reported even when there is invasion of the spine or metastasis to the liver. It seems that malignant tumours of the sympathetic nervous system occasionally undergo a spontaneous evolution to a more adult form of tissue and develop into a more or less inert gangliomatous mass. This curious, unpredictable and inexplicable metamorphosis is probably responsible for nearly all, if not all, the cures reported following this disease as they appear to be equally likely (or unlikely) after operative removal, biopsy only or X-ray therapy even in minimal dosage.

The neuroblastoma, arising as it does from primitive and undifferentiated tissue, is without functional activity. The tumour known as phaeochromocytoma, which is accompanied by paroxysmal hyperadrenalinism, is rare in adults and almost unknown in children (but see p. 445).

One child with a malignant tumour of sympathetic origin exhibiting these symptoms has been recorded at The Hospital for Sick Children, Great Ormond Street, during the last twenty-five years, and is still alive some years after biopsy only. Ganglioneuromata are not uncommon but are not, of course, malignant tumours.

Neuroblastoma is a tumour sensitive to X-ray therapy but incurable thereby. As has been noted, "cures" after X-ray therapy are no more frequent than after biopsy alone or after intercurrent infection with the exanthemata. The treatment is removal of the tumour when practicable and if there are no recognizable metastases. X-ray therapy should be reserved as a palliative for an occasional patient in whom pain or particularly distressing pressure symptoms may be relieved. The prognosis is hopeless except for a very occasional cure or spontaneous regression. Regression is more likely in tumours of other than adrenal origin. The average duration of life from the first symptom is from three to six months.

The Hutchison type (presenting with orbital metastases—discoloration, orbital swelling and proptosis) and the Pepper type (presenting with hepatic or glandular metastases) (fig. 630) are interesting and conspicuous clinical pictures but have no more significance than that. It should perhaps be reiterated here that "retroperitoneal sarcoma" is not a specific disease. The great majority of patients in whom such a diagnosis has been made have been suffering from neuroblastomata.

Wilms' tumour (Embryoma of kidney or nephroblastoma).—Next on the list in order of frequency is Wilms' tumour—one of the most specific of neoplastic diseases. Full discussion of its histogenesis is impracticable here. It most probably represents an aberration of growth beginning in the metanephros. It, also, is a tumour of very early years occurring in a series of sixty-one cases as follows:

0–1 (7) 1–2 (12) 2–3 (18) 3–4 (8) 4–5 (4) over 5 (12).

It is probable that the disease begins in the embryo during the development of the kidney. It has been described frequently in the fœtus. The presenting symptoms are: abdominal tumour or swelling (45 per cent.), hæmaturia (20 per cent.), pain (17 per cent.), malaise (10 per cent.), and vomiting (8·5 per cent.). The pre-eminent position of the first of these demonstrates the insidious nature of the onset. Pain, malaise and vomiting are secondary to the presence of the tumour and directly caused by it. Hæmaturia when it occurs (and this happens more frequently than is often stated) is frank bright hæmaturia and is due to venous pressure and capillary rupture and not to involvement of the pelvic mucosa. It is therefore similar in origin to the bleeding from congenital cystic kidney. An occasional association with infection of the urine may mislead the clinician. Hæmaturia in a child, as in the adult, demands full investigation of the urinary tract. The clinical finding is that of a tumour in the upper abdomen and loin (this was absent in only one of sixty-one cases). This tumour is smooth or slightly lobulated and of firm or variable consistency (fig. 632). There is usually a suggestion of mobility and it is often large in proportion to the size of the child. The general condition is

often surprisingly good, usually much better than in patients with neuroblastomata of similar size. There is usually no pyrexia, anaemia is not conspicuous, and there is seldom any evidence of metastases. The diagnosis may sometimes be made with some confidence on the history and the clinical findings, but investigation of the records shows how difficult it often is for the clinician to distinguish an embryoma from an adrenal neuroblastoma, an enlarged spleen, an hepatic neoplasm or other renal swellings. Further investigation of the renal tract and especially pyelography usually enables the correct diagnosis of neoplasm of the kidney to be made. Even the latter investigation may be misleading, however, as the renal pelvis may be deformed into a crescentic pattern by

FIG. 632.—MALE, AGED TWO MONTHS. WILMS' TUMOUR.

pressure from, or invasion by, a neuroblastoma or external pressure from other tumours, even intraperitoneal in origin (*e.g.* an ovarian tumour). Ascending pyelography is preferable to the intravenous method and is practicable almost from birth in the female and from one year onwards in the male. Alternatively intravenous pyelography, if necessary after surgical exposure of a suitable vein, usually gives a good X-ray picture if sufficient quantity of opaque material is used. In the very young a satisfactory picture may be obtained by the intramuscular route providing that hyalase is added to the diluted dose and that it is injected over a wide area or in divided doses to promote absorption. The pyelogram shown in fig. 632A was taken in a child of eighteen months by this method and shows normal renal pelvis separated from the abdominal tumour mass whose outline can be detected by the calcification in it. This tumour had been thought, because of its smoothness and the good general condition

of the sufferer, to be an embryoma, but this X-ray corrected the diagnosis to that of neuroblastoma.

Once the diagnosis is established beyond reasonable doubt, and this is a matter of great urgency, immediate nephrectomy should be attempted. The tumour is radio-sensitive though incurable by radiotherapy and if removal proves impracticable (a decision which can only be made at exploration) radiotherapy may reduce the size of the neoplasm sufficiently

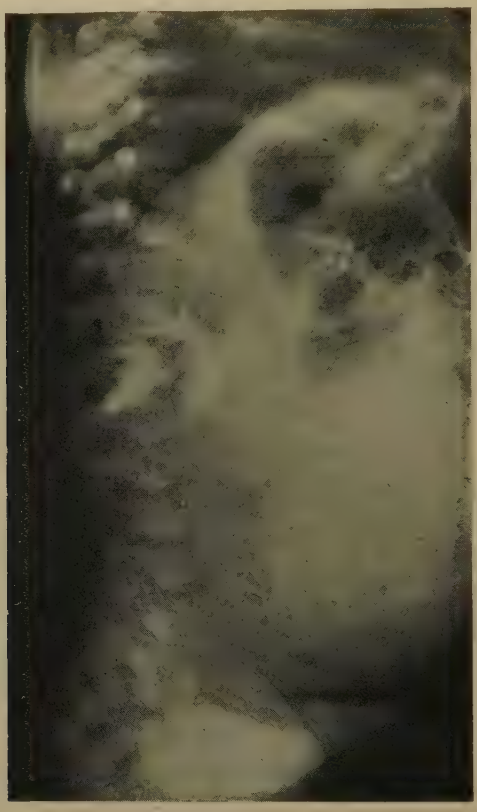

FIG. 632A.—INTRAMUSCULAR PYELOGRAM WITH HYALASE. CHILD, AGED NINE MONTHS. NEUROBLASTOMA WITH CALCIFICATION.

to make a second operation successful. It is doubtful if any case is cured in these circumstances and therefore primary removal should be the treatment of choice. If the child is unfit for even an attempt at removal it is unlikely that radiation therapy will help. Without removal of the tumour the prognosis is hopeless so that almost any operative risk is justified. In spite of the malignancy of the tumour and its usually large size when first seen the immediate results of operation are amazingly good. This is made possible by the relation of the growth to the kidney and its environment. There is sufficient encapsulation to assist removal until a

very late stage. Unfortunately the end results do not fulfil early hopes. In the series of sixty-one patients already referred to ten were considered unfit for operation, one died under X-ray treatment and the remaining fifty were operated on either as the primary treatment or following X-ray therapy. Twelve were irremovable, thirty-eight were removed and there were two operative deaths. Of the thirty-six survivors only four are alive and well more than five years after operation (and of these none had any X-ray therapy). Ladd and Gross are able to report nine five-year cures, none of which had any radiation before or after operation. Nothing appears to give any reliable clue to prognosis. A slightly more favourable prognosis in the youngest children seems due only to the fact that these

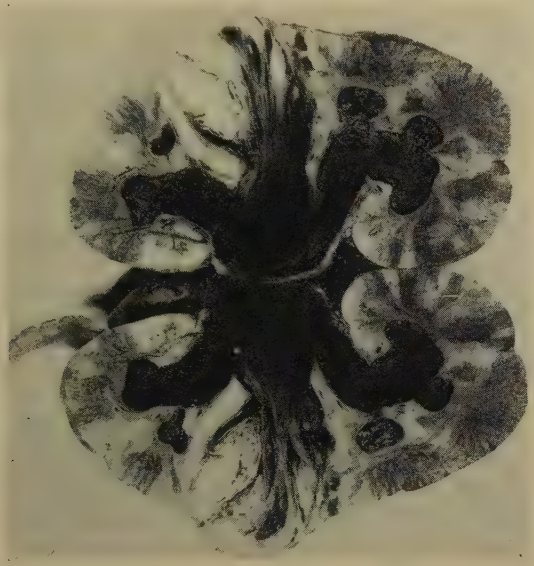

FIG. 633.—WILMS'S TUMOUR SHOWING HÆMORRHAGE INTO RENAL PELVIS.

are also the youngest tumours. The history, clinical and operative findings, and histology provide no further aid. The surgeon can only remove the tumour and hope for the best.

It is possible that this picture could be slightly improved by reducing the amount of abdominal examination to which the child is subjected and the speeding up of the primary treatment (nephrectomy) when once the presence of the tumour has been recognized.

Post-operative X-ray therapy has been extensively tried and there is evidence that it postpones recurrence. Its administration requires a long period of discomfort for the child and as it does not increase the cure rate at all it should not be used. X-ray treatment without operation cannot cure the patient.

Recurrence is usually rapid—within six months –but after X-ray therapy it has been postponed as long as three to five years. If a child is

alive and well two years after operation alone a cure is almost certain. Recurrence may be local, glandular or pulmonary. Metastases in liver and bone occasionally occur. An X-ray of the chest should precede operation. Treatment for a recurrence is not justifiable. Any slight increase in the child's expectation of life is valueless without the possibility of a permanent cure. A curious feature of post-operative metastases is the unusually high proportion occurring in the lungs. Probably this is due only to the slightly prolonged survival period, although manipulation before and during the operation may be a factor. It may therefore be reasonable to administer radiotherapy for a short period as a preoperative step in reducing this risk during the operation.

Very rarely other malignant tumours of the kidney have been recorded in children—adenocarcinoma or carcinoma of the renal pelvis. They are so uncommon as to be inseparable clinically from the more usual embryoma, and their treatment is the same whilst the prognosis is a little better.

Soft tissue sarcomata. Although rare in the particular this group of sarcomata accounts in the aggregate for a respectable proportion of all malignant tumours in children. If lymphosarcoma be included the total is about 15 per cent. Soft tissue sarcomata may be lipo-, myxo-, leiomyo-, rhabdo-sarcomata or synoviomata according to the tissue of origin. It is in this protean group that diagnosis is particularly difficult on clinical grounds and in which well planned surgical treatment, when practicable, may result in a cure. As with the carcinomata the possibilities are so numerous that little more than the barest outline can be given (fig. 634–638).

The tumour is almost always visible and palpable except when occurring in the alimentary tract, thorax or bladder, in which cases obstructive or irritative symptoms may be primary. When visible it is softish or firm, variable in definition but tending to be diffuse and gradually increasing in size. Occasionally signs suggesting sub-acute inflammation may be present but these are unusual. Pain is slight or entirely absent. The condition is usually mistaken for a sub-acute or chronic inflammation or for a cyst, hæmatoma or simple tumour. If there is the slightest unusual feature about such a swelling either in origin, on examination, or in clinical course a generous biopsy should be done. If the condition proves to be a malignant tumour complete removal offers a reasonable prospect of cure. In deciding the extent of operation to be performed considerable judgement and the most expert histological assistance are required. A fibrosarcoma or a myogenic sarcoma is often cured by generous local excision including the whole of the muscle of origin and its fascial sheath. In other cases amputation is required. In fibrosarcomata all degrees of malignancy from simple fibroma to the most malignant of metastatizing fibrosarcomata may be encountered. They may occur anywhere in the body but are perhaps a little more common in the limbs. Liposarcomata occur most frequently in the trunk—in the inguinal, scapular or contiguous regions or about the face. Surgical removal may therefore present particular difficulty. Nevertheless it should be attempted, for, although the condition is radiosensitive, recurrence is the rule. Recurrence when

FIG. 634.—FEMALE, AGED FOUR MONTHS. FIBROMA OF NOSE.—TWO LATER RECURRENCES.

FIG. 635.—MALE, AGED THREE WEEKS. SARCOMA OF FACE.

FIG. 636.—MALE, AGED TWO YEARS. SARCOMA OF CHEEK.

FIG. 637.—FEMALE, AGED SIX YEARS. LIPOSARCOMA OF EYELID (RECURRENCE).

FIG. 638.—FEMALE, AGED SIX YEARS. FIBROSARCOMA. RECURRENCE IN SCALP AND METASTASES IN NECK.

it occurs is primarily local though glandular and blood-borne metastases do occur especially after repeated incomplete excisions. In all cases secondary operations for local recurrences are permissible and indeed offer the only prospect of a cure. When the recurrence occurs in a limb, amputation is usually necessary. Soft tissue tumours of myogenic or lymphoid origin may occur in the intestine. They present as obstructions or as intussusceptions and removal has sometimes resulted in a cure. In all these conditions post-operative radiation has often been used, particularly when the surgeon feels uncertain about the extent of his operation, but should not be contemplated. If surgery has been inadequate, radiation may conceal the need for a more radical procedure. If such a procedure is impracticable, radiation will not cure. As in other similar conditions an exception may be made when the X-ray therapy aims at the relief of particularly distressing symptoms.

FIG. 639.—MALE, AGED FOUR YEARS. FIBROSARCOMA OF ANAL MARGIN.

Malignant hæmangioendothelioma.—This is a soft or spongy tumour which occurs especially in subcutaneous or sub facial situations. Usually its slow but steady growth invites surgical intervention. Its edges are ill-defined and operation findings, especially the lack of any attempt at encapsulation, suggest a tumour of local infiltrative powers. It is almost fleshy in consistency and pinkish in appearance. Removal should include a zone of macroscopically normal tissue and if this is done a cure often results. Simple lipohæmangioma, a moderately common tumour, may present a similar appearance, but there is usually a suspicion of surface discoloration and little if any alteration in size even over a long period. This description fits the two cases of this condition observed in children by the author. Both of these are alive and well following treatment by wide surgical excision followed by radiation.

Information regarding the pathology and behaviour of angiosarcomata is, however, confusing and incomplete. A recent review of the material from the Memorial Hospital, New York, suggests that an angiosarcoma is a very vascular and highly malignant lesion (only 9 per cent. of five-year cures). In this series of patients it occurred particularly in the limbs or head and neck and was sometimes preceded by trauma and sometimes developed in a pre-existing benign lesion. The authors advise very radical surgery, *e.g.* amputation when a limb is the affected part, and palliative radiation therapy in the inoperable head lesions.

Malignant melanoma.—Pigmented moles, benign melanomata, are common in children and may be present before birth. During childhood

they show evidence of active growth and increase of pigmentation, visible and microscopic. This activity may be so great that histologically it is indistinguishable from malignancy, but true malignant melanoma is unknown in children (except that very rarely it may arise in the eye).

Fig. 640 and 641 show a large melanoma on the back of a small boy. From birth it grew very rapidly, nodules of growth appeared above the skin surface and some even ulcerated. Tumour tissue was examined by

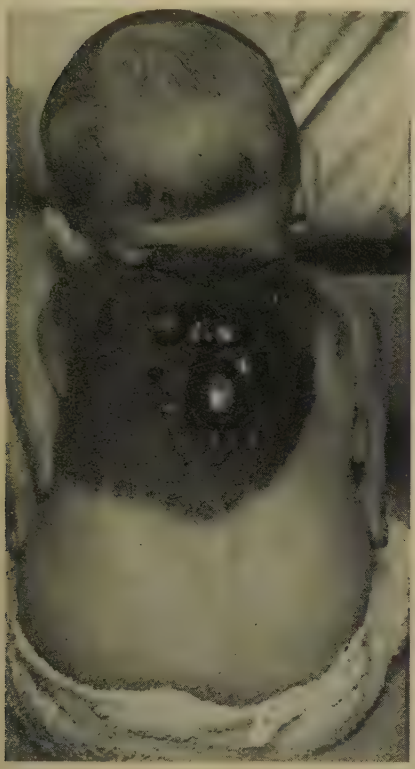

FIG. 640.—MALE, AGED THREE MONTHS. SO-CALLED MALIGNANT MELANOMA OF BACK.

FIG. 641.—SAME CASE AS IN FIG. 640 AFTER TREATMENT BY EXCISION AND SKIN GRAFTING.

several competent pathologists, all of whom pronounced it extremely malignant. The tumour was largely, but incompletely, excised segment by segment and during the course of treatment histological examination confirmed the gradual and natural change of the tumour to the innocent and benign lesion.

This matter is dealt with with some firmness because of the frequency with which a surgeon will be confronted with the histological suggestion of malignancy and the possibility, if the true life history of the melanoma in the child is not understood, that he will be persuaded to undertake unnecessarily mutilating and perhaps dangerous surgery.

Melanomata are so common and continue to appear with such ubiquity that extirpation of all lesions to prevent malignant change is just not practicable even if it were advisable. In the past it has been considered unwise to tamper with melanomata. In children there is no cause for alarm and if a melanoma requires to be removed for cosmetic reasons or because it is in a position in which it may be subject to repeated trauma local removal can be undertaken with perfect safety. It seems that malignant change in melanomata requires post-pubertal hormonal assistance.

Kaposi's hæmorrhagic sarcoma is a condition of obscure ætiology, but it is almost certainly not a true neoplasm. Some cases so recorded may be examples of malignant disease of lymphoid origin.

Rhabdomyosarcoma.—Besides a very occasional occurrence in striped muscle, *e.g.* the tongue, palate or skeletal musculature, malignant tumours showing the characteristics of rhabdosarcomata occur in the region of the bladder neck, the vagina and the gonads, and they are briefly described in the next two paragraphs.

Sarcoma of the prostate and bladder.—Numerous cases of sarcomata occurring in the bladder and prostate have been recorded in infants. These tumours are of embryonic nature, arise in the prostate and bladder neck, and show rhabdosarcomatous characteristics. They are comparable with "sarcoma botryoides" and probably arise in the mesenchyme in its immature stage rather than in the scanty striped muscle fibres in the neighbourhood. Until recently almost all have been treated with radiation with uniformly fatal results. In the last edition it was suggested that a complete extirpation of the bladder and prostate with transplantation of the ureters, although a hazardous procedure, might offer the prospect of a cure. Recently this operation has been successfully practised in a few patients (p. 1614).

FIG. 642.—FEMALE, AGED FOUR YEARS. SARCOMA BOTRYOIDES.

Sarcoma botryoides.—This is a very malignant tumour arising in the vagina or uterus (usually the vagina), occurring in infants and presenting with vaginal hæmorrhage and discharge. A polypoid, fleshy, hæmorrhagic growth forms in and eventually projects from the vagina. Extension into the pelvis produces interference with micturition and an abdominal tumour. The condition is prob-

ably an rhabdomyosarcoma of embryonic origin. Although the tumour itself is very malignant, spread to the regional lymph nodes and distal metastases are relatively uncommon. For this reason the condition is theoretically curable by radical surgery. This was attempted over fifty years ago but was unsuccessful until recently. A successful case was reported by Meigs in 1947 and another by Shackman in 1950. Needless to say the operation is extensive and mutilating. It is therefore fortunate that the condition is very rare. No cure has ever been reported from radiation therapy.

Embryonic tumours.—These tumours combine malformation with new growth. Their true nature and genesis is incompletely known. A malformation is an anatomical error arising during the development of the body to its full state (Willis). This definition is shared by some tumours, even malignant tumours, which arise as disturbances of development in immature tissues and due presumably to some metabolic abnormality in the tissues themselves. The commonest malignant embryonic tumours are those of the brain, retina, and kidney which are described separately. Embryomata are also occasionally recorded in other sites.

Hamartoma.—This term is used to describe superfluous tumour-like masses of improperly blended tissues. Angiomatosis and neurofibromatosis are the best known examples of this condition, but a variety of isolated lesions answering to its definition have been recorded in various situations —lung, liver, intestine, connective tissue, and elsewhere. The hamartomata are not true tumours, but the dividing line between a hamartoma and an embryoma may be difficult to draw. They are mentioned here because, when occurring as an isolated lesion, a hamartoma is almost certain to be considered a tumour. Its size is often considerable and the symptoms it produces often dangerous, for instance intestinal obstruction or bleeding from the bowel. The occasional occurrence of such lesions is an additional argument in favour of exploration of unusual tumours before accepting a hopeless prognosis. Successful removal of hamartomata and embryomata has been recorded from a variety of situations, even from the liver and lung.

Lymphosarcoma.—The widespread distribution of lymphoid tissue in the body suggests the possibility of a wide variety of clinical pictures if malignancy should arise in this tissue and this is certainly confirmed in practice. So varied are the findings that the diagnosis is hardly practicable on clinical examination. Most commonly the first sign is enlargement of the lymphoid tissue in the neck or the thymus, presenting as a soft to firm swelling in the neck or by symptoms of mediastinal pressure – dyspnœa, cough and enlargement of veins. The tumour may show itself first in lymphoid tissue elsewhere—nasopharynx, tonsillar region, abdomen or groin. When occurring in the nasopharynx it must be distinguished from the rare recurrent fibroma of that region. Occasionally the primary tumour may be found in situations where no aggregation of lymphoid tissue is to be found, *e.g.* on the back.

In most cases the diagnosis can only be suspected by exclusion of other conditions, leukæmia, lymphadenoma, infective lesions or other

intra-thoracic lesions, and proven only by histological examination before or after death. When once the disease has begun the lesions rapidly become widespread and death occurs from exhaustion though often with the patient in a surprisingly good state of general nutrition. Besides the widespread lesions in lymphatic tissue in the usual situations infiltration of other organs bone, intestinal tract, skin or other viscera—may occur. The disease is rapidly fatal usually within a few months. It is probable that the disease is potentially widespread from the start as with other malignant lymphadenopathies of obscure ætiology. In fact, as has been mentioned, both leukæmia and Hodgkin's disease are forms of sarcoma of lymphoid origin. Cures have been reported but they are so rare and so little in keeping with the pathology that the diagnosis must be doubted. No treatment offers any prospect of a cure in a proven case. Once the diagnosis is established there is only palliative treatment by radiation perhaps supplemented or replaced by nitrogen mustards or other chemotherapeutic agents. All these compounds, however, are very toxic and careful consideration must be given to each patient before deciding whether the benefit is in fact likely to outweigh the unpleasant side effects.

Hodgkin's disease.—This is discussed on page 1104.

Hepatoma.—This rare tumour is of diagnostic and pathological interest only (but see also hamartoma). The sufferer is usually a young infant, most cases occurring under the age of one year. As the tumour when recognized is of large size it is probably present from early embryonic days. It appears to be unrelated to the hepatoma of adult life in which cirrhosis is an ætiological factor and its histogenesis is still a matter of debate. Possibly some are embryonic in origin (hepatoblastomata) and these show an admixture of entodermal and mesodermal components. Others are primary carcinomata of adult type occurring in children. Both are malignant tumours and metastases may occur in lungs, peritoneum or glands. Clinically a hepatoma presents as a firm, smooth or slightly irregular tumour in the right hypochondrium, often recognizably in the liver but sometimes mistaken for a tumour in the loin. The differential diagnosis is from Wilms's tumour or from primary or secondary neuroblastoma ; the final diagnosis is usually made only after laparotomy or in the post-mortem room.

Osteogenic sarcoma

A considerable literature has accumulated on the subject of osteogenic sarcoma, but the number of cases likely to be seen by one clinician in a lifetime will be small and even the accurate documentation available does not enable him to have a clear-cut idea as to the prognosis and treatment in an individual case.

Diagnosis.—The disease is conspicuous in its symptoms and signs and, although there are difficulties in the diagnosis, these can almost always be solved by a biopsy. It is distressing to know that delay in diagnosis often combines with the great malignancy of the disease to make the prognosis gloomy. The earliest symptom is pain of an aching or boring

OSTEOGENIC SARCOMA IN CHILDREN (under 15)

Series.	No.	Treatment.		Cured (5 years or more).
Geschickter and Copeland	93	Surgery alone	57	13
		Surgery plus radiotherapy	4	1
		Radiotherapy alone	13	1
		Surgery plus toxins	2	1
		Miscellaneous treatment and no treatment	17	1

character, often following injury, to which the lesion is frequently but probably wrongly attributed. The duration of the pain, as Codman puts it, is one of months, not days, weeks or years. It is constant in situation, becomes steadily more persistent and more severe. Later function of the limb may be interfered with. Usually a swelling appears, of slow growth and of variable physical appearance, usually firm, not tender and as a rule

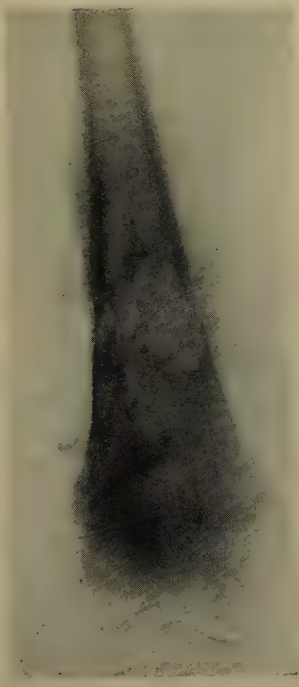

FIG. 643.—FEMALE, AGED ELEVEN YEARS. OSTEOGENIC SARCOMA OF FEMUR.

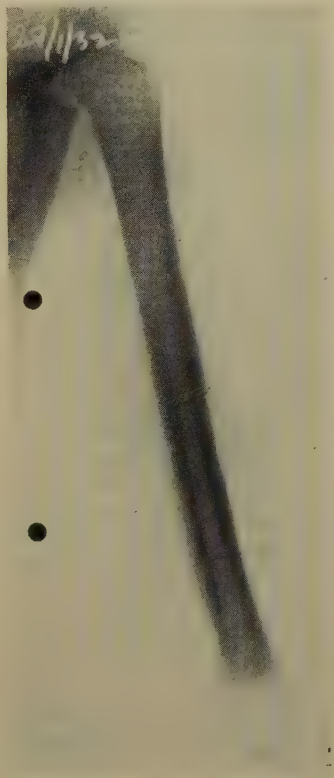

FIG. 644.—MALE, AGED SEVEN YEARS. OSTEOGENIC SARCOMA OF HUMERUS (SHOWING RADIOLOGICAL APPEARANCES USUALLY DESCRIBED AS TYPICAL OF EWING'S TUMOUR).

showing little evidence of inflammation, though in some cases (particularly the osteolytic type) the warmth, redness and even the tenderness and pyrexia of inflammation may be present. Occasionally but rarely pathological fracture may occur. The lesion is most common in the region of the knee joint. After that in frequency comes the upper end of the humerus and the pelvis. The remainder may occur in any bone. The final diagnosis is reached by history, clinical and radiological examination, and by biopsy. Osteogenic sarcoma must be distinguished from osteo-

FIG. 645.—BONY METASTASIS FROM NEUROBLASTOMA RESEMBLING OSTEOGENIC SARCOMA.

FIG. 646.—BONY METASTASIS FROM A RETINAL NEUROBLASTOMA RESEMBLING OSTEOGENIC SARCOMA.

myelitis, syphilis of bone, Ewing's tumour, metastatic lesions (especially neuroblastoma) (fig. 645) and, with diminishing likelihood of confusion, lipoid histicytosis, leukæmic or lymphadenomatous deposits, scurvy and Cooley's anæmia.

No classification into subgroups can relate perfectly the gross and the histological features and none is of value in deciding treatment so they will not be discussed here. It is best to follow Bradley Coley and to use the terms osteogenic sarcoma, chondrosarcoma and fibrosarcoma of bone (the prognosis in the last group being appreciably more favourable). The histological appearance of the resected lesion is the best guide to prognosis.

An osteolytic lesion may give most difficulty in diagnosis for it may be closely mimicked by osteomyelitis, Ewing's tumour or metastases. A sclerosing lesion may give an X-ray appearance similar to that of syphilis. The X-ray appearances are in general those described by Codman: medullary and periosteal involvement, old cortex or its remnants in the normal position (erosion of bone and not its expansion), osteolytic and osteoblastic changes together, shadow of invasion of soft tissue and subperiosteal reactive triangle. No one of the signs belongs to osteogenic sarcoma alone and one or more may be absent. Errors in diagnosis resulting in unnecessary or useless amputations have been made even after the most careful clinical investigation and no limb should be removed without histological confirmation of the disgnosis. The final appeal must therefore be to histological examination by biopsy.

TREATMENT.—In spite of confusing literature the proper course to adopt is clear and the prognosis, though poor, is by no means hopeless. Bradley Coley reported 21·9 per cent. of five-year cures in 342 cases of all ages from the New York Memorial Hospital, though in this series the survivals in those cases occurring under the age of fifteen are very few. Coley agrees that although operation gives such a poor prognosis no other form of treatment offers the least prospect of a cure. Although Coley finds a particularly unfavourable prognosis in cases of osteogenic sarcoma in young children, the very large series of Geschickter and Copeland shows no significant difference in prognosis when decade is compared with decade. Indeed, of their eighteen cases under the age of ten no less than seven are cures of five years or more, six from surgery alone and one from surgery plus radiation (see also p. 1891). The only present chance of successful treatment lies in early diagnosis and operation. Earlier recognition of suspicious symptoms results in the discovery of less conspicuous and therefore less definite radiological appearances. Delay is inexcusable. If there is any suspicion of malignancy a second opinion should be taken, the position explained to the parents and immediate operation carried out providing that the removal of the diseased bone is practicable. The first step of the operation is the taking of a portion of the tumour for examination by frozen section. If possible this is done between tourniquets to avoid any possibility of venous contamination. Such an authority as Bloodgood does not think that biopsy with delay before definitive operation is dangerous. If therefore the frozen section is indefinite (and this is rare) a short delay is permissible to permit examination by other methods. Although the incision into the tumour may not increase the danger, the delay itself in a disease of so short a natural history does and should be avoided if possible. Metastasis from osteogenic sarcoma is

FIG. 647. MALE, AGED SIX YEARS. SARCOMA OF ZYGOMA.

almost confined to the lungs. Metastasis to lymph nodes and other bones is reported, but is so rare that for practical purposes it may be ignored. Amputation need be done only an adequate distance above the tumour, *e.g.* site of election for growth in the lower tibia or upper thigh for growth in the lower femur. Extra mutilation does not improve the prognosis.

X-ray therapy is justifiable in lesions which cannot be extirpated. It reduces pain and may permit a more or less comfortable death from pulmonary metastases rather than from pain, exhaustion and fungation of the primary lesion. It should never be used as an alternative to surgery when surgery is practicable. For metastases it is useless nor should it be employed, as is sometimes advised, as a preliminary to surgery. Operation should not be undertaken without X-ray examination of the chest, though the presence of pulmonary metastases does not necessarily contra-indicate a palliative amputation in order to spare the patient the suffering caused by the primary tumour.

Results are poor : 10 to 20 per cent. are cured. Although bad this is good enough to make operation worth while whenever practicable. Earlier diagnosis and therefore speedier treatment may improve the prognosis to an appreciable extent. The natural history of the disease is a short one (one to three years) but is variable. It is not increased by an operation which does not result in a cure. Occasionally the pulmonary metastases may be slow in growth and death may occur only after their presence for one to two years. The presence of these metastases is recognized by routine X-ray examination or at a later stage by the coughing up of blood-stained sputum, or occasionally by their presentation through the chest wall. Local recurrence is almost unknown and its absence is strong argument in favour of moderation in the extent of surgical removal.

Ewing's tumour (endothelioma of bone). This small subject is beset with clinical difficulties and pathological controversy. Its frequency has been variously stated but is often given as about 10 per cent. of malignant bone tumours. Half the cases are said to occur in children. Efforts have been made to describe the disease as a typical entity. This is not so. It may occur in almost any bone and any slight preference for individual sites is of no value to the clinician. All the symptoms and signs—pain, tenderness, pyrexia, leucocytosis and a fusiform or diffuse swelling of the affected bone may be associated with one or other of the lesions from which it has to be distinguished (fig. 644). Radiological appearances are largely those of bone destruction but subperiosteal reaction may be quite conspicuous and sometimes the lesion may appear sclerotic (*e.g.* in the os calcis). The changes appear to begin in the medullary region. The differential diagnosis is from osteomyelitis, secondary neuroblastoma and osteogenic sarcoma. Most of the cases diagnosed as Ewing's tumour are actually one or other of these. Willis believes that most are secondary neuroblastomata. Whilst this is true in most cases which are fully investigated in the post-mortem room, an occasional primary lesion of medullary origin is proven. Such cases occur in older children and are much less than the 10 per cent. they are said to be.

The diagnosis can only be made by biopsy. Even this may be indefinite or controversial but it excludes an inflammatory lesion and by so doing allows legitimate treatment to be proceeded with. It is said that the disease is liable to produce metastases in other bones (unlike osteogenic sarcoma), but these cases are almost certainly secondary tumours.

TREATMENT.—In deciding on treatment it must be borne in mind that the diagnosis of endothelioma of bone cannot be made with certainty. Inflammation having been excluded by histological examination there still remains the possibility that the lesion is one of three things—a true endothelioma of bone, an unusual osteogenic sarcoma, or a secondary neoplasm. An attempt is made to exclude the last possibility by a search for the primary tumour or other metastases. If either is found treatment

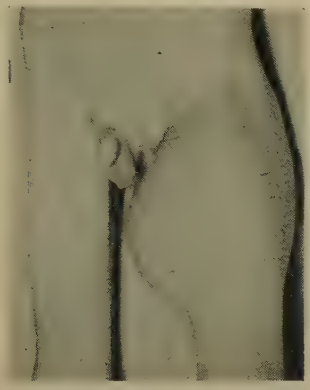

FIG. 648.—MALE, AGED EIGHT YEARS. EWING'S TUMOUR —L. FEMUR.

FIG. 649.—MALE, AGED TEN YEARS. EWING'S TUMOUR —RIBS.

is palliative only and radiation has its place in the reduction of pain and the prevention of pathological fracture. If there is a reasonable chance that the tumour is solitary the treatment is immediate amputation. Radiation has been recommended as a diagnostic procedure but common sense alone shows the lack of justification for this. The prognosis seems almost hopeless, but is difficult to assess with exactness because many metastatic lesions are inadvertently included in almost any series. The real Ewing's tumour is occasionally curable by surgery.

Other malignant tumours in bone.—Very rarely a *periosteal fibrosarcoma* may occur in a child. Its clinical picture closely resembles that of osteogenic sarcoma and its treatment is the same. The prognosis is very much better.

Adamantinoma of long bones.—Two of the eighteen cases of this rare condition reported in the literature up to 1942 occurred in children under fifteen years old.

Chloroma (another very rare condition) is not a true tumour of bone but a metastatic leukæmic lesion.

Multiple myeloma does not occur in children and can therefore be excluded from the differential diagnosis.

Chordoma, another extremely rare tumour, has been recorded in childhood. Harvey and Dawson in 211 cases found fourteen in the first and seven in the second decade. It is a soft, gelatinous, well defined tumour of variable though usually low malignancy and local invasive powers arising from notochordal remnants and occurring in the sacro-coccygeal, spheno-occipital or vertebral regions (51 per cent., 39 per cent. and 12 per cent. respectively in Harvey and Dawson's series). When occurring in the sacrococcygeal region it is usually anterior to the sacrum. Removal may be attempted but is seldom complete and the ultimate prognosis is very bad, though long survival periods have been recorded. Metastases are uncommon but in the only case at The Hospital for Sick Children, Great Ormond Street, in the last twenty years they were widespread.

FIG. 650.—FEMALE, AGED THREE MONTHS. SACRO-COCCYGEAL CHORDOMA.

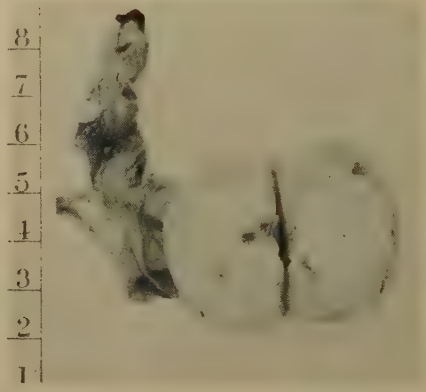

FIG. 651.—MALE, AGED THREE MONTHS. CARCINOMA OF TESTICLE.

Testicular tumours

Malignant tumours of the testicle in children are rare; innocent tumours are unknown. When carcinoma (fig. 651) occurs it is usually at an early age (before three years), although sometimes a malignant teratoma occurs in the later years of childhood. The differential diagnosis is from inflammation or from testicular swellings due to torsion or to pressure from a hernial sac. A firm tumour of the testicle with absence of sensation and no signs of acute inflammation or swelling of the cord is highly suspicious of malignancy. Operation is urgent and should be simple orchidectomy. In the treatment of this condition in children X-ray therapy has no place either prophylactically or for metastases when they occur, although in this latter case it may postpone the fatal termination

which is certain when they have shown themselves. Metastases may occur in regional nodes or in the lungs. Histologically the tumour is usually an adenocarcinoma of embryonal type representing a unilateral development in a teratomatous condition. Occasionally it may even be of chorionepitheliomatous type. The disease is almost invariably fatal, usually within twelve months but occasionally, especially if X-ray therapy has been used, after a longer period (four years in one case). Its deadly nature is due to its intrinsic malignancy combined with the fact that its rarity almost always leads to hesitancy in treatment. That the prognosis is not quite hopeless is shown by the history of the case shown in fig. 651. This child is alive and well six years after simple orchidectomy and is therefore almost certainly cured. The orchidectomy was performed less than a week after his first attendance at hospital.

The relationship of malignant disease to undescended testicle is always a question of debate. About one quarter of malignant testicular tumours occur in maldescended testicles. Malignant change does not occur in childhood but can rightly be considered a point in favour of the operative correction of this disability during that period. What is not known, however, is whether operative correction removes this slight potential towards malignancy. It may be assumed with some justification that malignant change in a testicle reduced to the scrotum by operation would be particularly likely to be reported ; as so little attention has been drawn to this point in the literature it is probable that the slight bias in favour of malignant change is removed by successful surgical treatment. Proof of this awaits a more comprehensive study.

Ovarian tumours

According to Ladd and Gross about 60 of the 100 or so ovarian tumours which have been recorded in children were malignant ; the remainder being cysts or dermoids. The malignant tumours may be fibrosarcomata (which is particularly uncommon), adenocarcinomata, granulosa cell carcinomata—presenting with precocious puberty, arrhenoblastoma giving rise to masculinisation, or dysgerminoma, a seminoma-like lesion. An abdominal or pelvic mass is almost always recognizable, and in cases of granulosa cell carcinoma or arrhenoblastoma is associated with endocrine disturbance. Pain is an uncommon symptom. The treatment is surgical removal when practicable. Distal metastases are late and uncommon in these tumours so that if primary lesion is removable there is a reasonable prospect of a cure. (For further consideration of the endocrine effects of these tumours see p. 458.)

Cortical adrenal tumours

A small number of cortical adrenal tumours which are usually malignant, though occasionally benign, have been reported in childhood. The tumour is rarely detectable by palpation and its presence is signalled by the appearance of its androgenic effects—precocious pubertal changes

FIG. 652.—FEMALE, AGED FOURTEEN MONTHS. EPITHELIOMA SKIN OF NOSE.

FIG. 653.—(SAME CASE AS FIG. 652). RECURRENCE IN GLANDS OF NECK.

FIG. 654.—REPRODUCTION OF SPECIMEN OF CARCINOMA OF COLON FROM GIRL OF TEN YEARS.

(F. D. Saner in *Brit. J. Surg.*)

FIG. 655.—BARIUM ENEMA OF SAME PATIENT

in the male and masculinisation (enlargement of clitoris and male distribution of pubic hair) in the female. In each there is some precocious bony development and there may be slight hypertension.

Whilst in some cases in male children the development, though abnormally precocious, is along approximately normal lines, in others the symptoms are those of Cushing's syndrome (see fig. 120, p. 441) with elevation of urinary steroids, abnormal fat distribution, and skin changes. In adults the differentiation between basophil adenoma of the pituitary and adrenal cortical neoplasm or hyperplasia may be extremely difficult. In children the basophil adenoma does not occur and all cases of adrenal syndrome should be explored.

The treatment of these lesions is surgical, and a reasonable proportion are curable thereby, the cure including disappearance of the androgenic effects. (See also p. 440.)

Carcinomata

Malignant tumours of epithelial origin are rare in childhood, but nevertheless there is hardly a single form of cancer common in adults which has not at some time or other been seen in a child. Cancer of the skin (fig. 652), the lip, the stomach, the buccal mucosa, cervix, bladder,

FIG. 656.—FEMALE, AGED SIX YEARS. CARCINOMA OF PAROTID. (Note facial palsy.)

colon (fig. 654), pancreas, parotid (fig. 656) and thyroid have all been recorded under the age of twelve, and many much younger. Even carcinoma of the breast, in which the postpubertal endocrine factor is particularly important, has been described in a child of eleven.

It would be impracticable to describe each and its treatment in detail.

In general their presentation is almost identical with that of the same condition in adults. If a typical cancer is seen in a child then it probably is a cancer. For instance a firm tumour of the parotid gland with a facial palsy means cancer (fig. 656). Procrastination in diagnosis because the

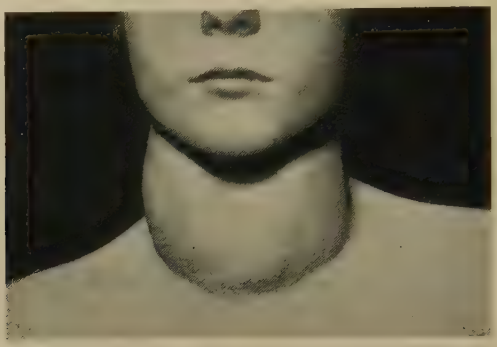

FIG. 657.—FEMALE, AGED TWELVE YEARS. CARCINOMA OF THYROID. (Case of the late Dr. F. J. Poynton.)

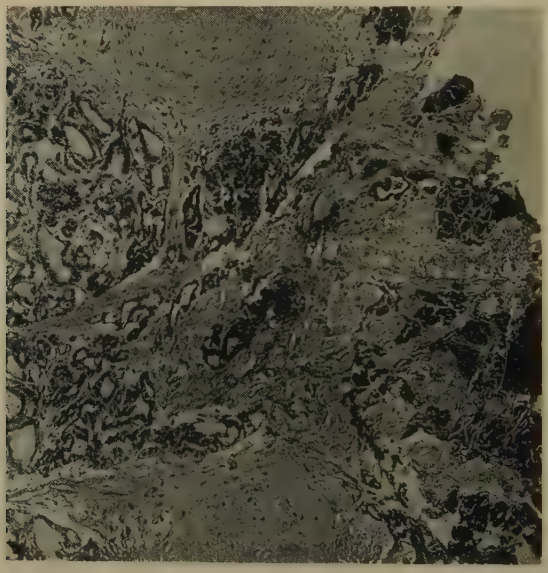

FIG. 658.—SAME CASE AS FIG. 657 SHOWING INFILTRATION OF TRACHEA.

disease is unlikely must be avoided. Unfortunately it is a common finding in the clinical histories of such cases. Once the condition is suspected, however remotely, the diagnosis must be confirmed or refuted by biopsy. It is often assumed that the course of a cancer occurring in childhood must be of dramatic ferocity, but this is not the case. The clinical course and the rate of growth closely resemble the same condition in an adult.

When the condition is confirmed as a cancer the treatment is radical surgery if practicable. Whereas in an adult it is right to weigh the prospect of a radiation "cure" of three, five or more years without complete elimination of the disease against the mutilation and mortality of direct surgical attack, in a child it is not. Every effort should be made to eradicate the disease at the primary treatment. Even in such a condition as carcinoma of the parotid a risky extirpation with the resulting facial paralysis is better than the dreary existence and ultimately fatal termination associated with radiation therapy. Courage and skill are necessary and sometimes are handsomely rewarded.

Xeroderma pigmentosum is a peculiar and fortunately rare condition in which the skin is intolerant of actinic radiation and responds to exposure to sunlight by the development first of pre-cancerous lesions and later of multiple carcinomata with an usually fatal result. Careful precautionary measures have enabled patients to survive well into adult

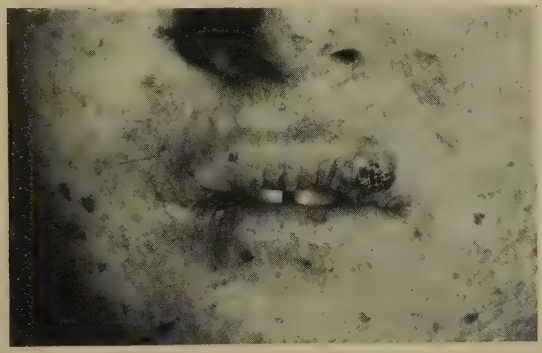

FIG. 659.—FEMALE, AGED EIGHT YEARS. EPITHELIOMA OF LIP OCCURRING IN XERODERMA PIGMENTOSUM.

life, and recently attempts have been made to provide protection against the carcinogenic effect of ultra-violet light by the use of cosmetic creams, which allow nearly normal activity. With such protection the patient in fig. 659 has already survived four summers without demonstrable change (Smithers and Wood, 1952).

Teratomata

It is not possible to do justice here to this fascinating pathological study. The main points are: Definition (Willis): "A teratoma is a true tumour or neoplasm composed of multiple tissues of kinds foreign to the part in which it arises." All teratomata prove to be tridermal if a careful enough search is made. They are specific tumours and not related to double monsters or malformed twins. They must be distinguished from quiescent masses of ectopic tissue, *e.g.* gastric mucosa in a Meckel's diverticulum, branchial cysts, reduplication of the gut and so forth in which no neoplastic growth occurs. The requirement that the tissues must be foreign to the

site and that the lesion is tridermal separates them from the embryonic tumours.

Distinction may be made between benign and malignant lesions but border line cases occur. Histological structure is a guide but not a certain one. The occurrence of embryonic elements in a real teratoma indicate malignancy.

They are most commonly found in the gonads, retroperitoneally, in the presacral (coccygeal) region, in the anterior mediastinum and at the base of the skull—very rarely elsewhere. In children they are most frequently found in the sacral region and retroperitoneally—occasionally in the other sites. They are usually congenital and benign, but occasionally malignant change is found. Girls are affected more frequently than boys.

It is now clear from the work of Nicolson, Willis and others that the tissue relationships in teratomata are not entirely haphazard but show evidence of the same co-ordinating factors which occur in normal organogenesis—for example cystic intestinal spaces are related to smooth muscle and nervous tissue to meningeal-like structures and cartilage and bone. This organogenetic effect is most completely seen in the formation of digits, teeth and recognizable portions of intestine and nervous system.

Sacrococcygeal teratoma.—This is usually present at birth as a bulky tumour of variable consistency—partly solid and partly cystic. It is nearly always posterior to the sacrum but occasionally anterior. Although they are most prominent posteriorly, their origin is in the presacral or precoccygeal regions. The relationship to the bone and periosteum is intimate and variable, but the bone is usually intact.

In this region there is much complex embryological activity connected with the neurenteric canal, the post-anal gut and the closure of the spinal cord. Tumours and cysts arising from these structures may be difficult to separate from true teratomata.

Sometimes the bulk of the tumour is found in the pelvis or projecting up into the abdomen. A similar lesion occurring a little higher still would be classed as retroperitoneal.

Epignathi and basal cranial teratomata, though almost never malignant, are almost always fatal in fœtal or neonatal life because of their situation and the impossibility of surgical removal.

Malignancy in teratomata.—This may occur in two ways :

(1) Unilateral malignant change in a previously benign growth – most often squamous or adenocarcinoma.

(2) Total malignancy. This occurs most frequently in testicular teratomata but occasionally in others. Metastases are also of composite structure.

In addition intraperitoneal transplantations may occur from histologically benign teratomata.

Treatment.—The treatment of teratomata is surgical because of their local effects and actual or potential malignancy. In a fairly high proportion of cases a cure results though the operation itself may be formidable and dangerous. If metastases occur following the removal

of a malignant teratoma they nearly always appear within two to three years.

Summary

In a series of conditions so diverse as malignant tumours in children it is not permissible to generalize to any extent but two conclusions may be drawn. The first is that accurate diagnosis usually requires histological assistance and the second is that treatment is surgical excision of the lesion as soon as possible. There is a tendency to consider radiation therapy and surgery as alternative forms of treatment which must be carefully weighed one against the other. In adult life there is often some justification for this, but in children the records show that, for all practical purposes, radiation cures do not exist, and in childhood the prolongation of existence without possibility of cure is seldom justifiable.

Acknowledgements

The illustrations in this chapter are largely from the photographic collections of The Hospital for Sick Children, Great Ormond Street, London, and the Royal Cancer Hospital, London. One or two are from the author's collection, and numbers 654 and 655 are by permission of Messrs. John Wright and Sons and F. D. Saner, Esq.

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APPENDIX

PRACTICAL PROCEDURES

JANET D. ROSCOE AND J. P. M. TIZARD

THE adoption of any technique must necessarily be a matter of some experience and personal idiosyncrasy. A foundation must be laid before variations can be made. There are certain general principles which it is well to remember before starting on the simplest practical procedure. The way in which help is desired from an assistant should be carefully explained. The nursing staff should not be left in doubt as to what is expected of them either during or after any operation. The duties of wrapping and holding the child are of the utmost importance. The quieter the child the easier will be the necessary interference. Much needless apprehension in the older child may be avoided by making preparations for the procedure out of his sight and by giving him a simple but truthful explanation of what is to happen. Infants may be quietened by a feed or something to suck. Local anæsthesia should be given when necessary. In all cases the question of giving a sedative must be carefully considered. Three conditions must be satisfied before starting any practical procedure:

(1) The lighting must be satisfactory;
(2) the instruments must be in perfect condition; and
(3) the child must be placed or held in the correct position.

Methods for the following procedures are outlined—

PARENTERAL FLUID ADMINISTRATION:

(*a*) Intravenous
(*b*) Bone marrow
(*c*) Subcutaneous
(*d*) Intramuscular
(*e*) Rectal
(*f*) Exchange blood transfusion

COLLECTION OF SPECIMENS:

(*a*) Blood
(*b*) Bone marrow
(*c*) Urine
(*d*) Cerebro-spinal fluid

STOMACH WASHOUT

ŒSOPHAGEAL FEED

DUODENAL SUCTION

INTRAMUSCULAR INJECTION

ARTIFICIAL RESPIRATION

INTRAVENOUS PYELOGRAPHY (p. 1588)

BRONCHOGRAPHY (p. 767)

Intravenous Drip Infusion and Transfusion

This method of administering fluid is particularly useful in restoring and maintaining body water and electrolytes when adequate fluid intake by mouth cannot be contemplated for some days and when considerable dehydration is already evident, as, for instance, for severe infantile diarrhœa and vomiting, intestinal obstruction, or in the treatment of shock from burns or other cause. Blood and plasma must be given by the intravenous route.

With sufficient practice it is usually possible to carry out intravenous infusion in infants and young children without cutting down on the vein by inserting the infusion needle through the skin. This should always be possible in older children.

The advantages of the percutaneous method are:

(1) That it avoids the necessity of an incision, which adds to the dangers of local infection and which results in scarring;

(2) That the vein is not tied and therefore remains available for subsequent infusion, and

(3) That the site of infusion can be changed every twenty-four or forty-eight hours, thus reducing the period of immobility of the limb and the risk of œdema and phlebitis.

The disadvantages of the percutaneous method are:

(1) That, as the needle is not tied into the vein, it is more likely to slip out during an infusion;

(2) That the sharp point may penetrate the wall of the vein during an infusion, and

(3) That it is usually necessary to use a needle of finer bore than a Bateman's cannula thus increasing the possibility of blocking by blood or plasma.

Because of these drawbacks the percutaneous intravenous infusion necessitates more constant nursing care than does the cut down. A cut-down infusion is preferable if, for instance, the child has to be moved to the operating theatre.

Procedures.—(*a*) PERCUTANEOUS METHOD.—It is best to choose a site where the veins are superficial and where there is little subcutaneous tissue. In infants and young children veins on the dorsum of the foot or hand, the dorsal or palmar surfaces of the wrist or the scalp and in older children veins on the dorsum of the forearm or in the antecubital fossa will be found most suitable. The transfusion set is arranged and the limb splinted or the head held as described in the next sections.

A hypodermic needle with a short bevel is used, the gauge of the needle depending on the size of the vein (even in infants this need not usually be

(*a*) Inner cannula. (*b*) Outer cannula.

FIG. 660.—BATEMAN'S NEEDLE.

smaller than a No. 12 hypodermic needle). The needle is fixed (not too firmly) to a 2 c.cm. syringe almost filled with normal saline solution. The veins are engorged by proximal pressure of a rubber tourniquet or, better, a sphygmomanometer cuff inflated to approximately the diastolic pressure. The skin over the vein should be stretched and held taut by a piece of

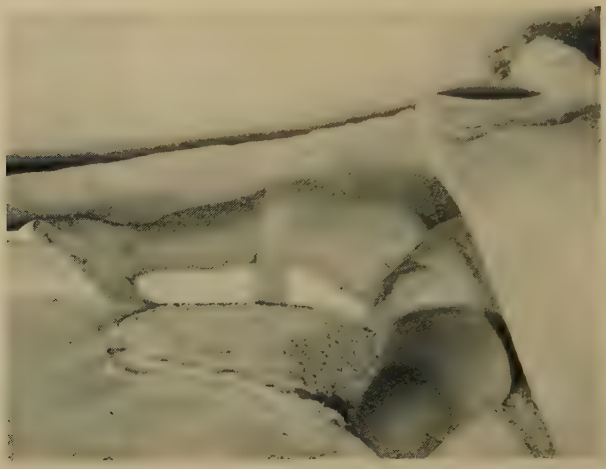


FIG. 661.

FIG. 662.

FIG. 661 AND 662.—SPLINTING OF LIMB FOR INTERNAL SAPHENOUS VEIN.

adhesive strapping distal to the site of puncture. After sterilizing the skin the needle is introduced above the line of the vein. The vein is often deeper than it appears. When the needle lip is judged to be against the vein wall, a short jab will cause it to penetrate and the needle is then threaded one or two centimetres up the vein. If the needle is gently moved from side to side, the whole vein will be seen to move with it. That the needle is in the vein may be confirmed by withdrawing the plunger

of the syringe. However, it is not always possible to withdraw blood from small veins and, if this is the case, a little saline is cautiously injected. If the needle tip is outside or within the wall of the vein a subcutaneous swelling appears. If no swelling occurs the syringe is gently removed from the needle and replaced by the adaptor of the infusion set.

With the aid of gauze swabs and adhesive strapping the direction and elevation of the needle are adjusted to produce the most rapid flow of the infusion fluid. The rubber tubing is secured to the limb and splint and a loop made as shown in fig. 669(*a*), so that an accidental jerking of the limb or infusion stand will be less likely to result in the needle being dislodged.

If a scalp vein is used for continuous drip infusion the difficulty of fixing the needle may be overcome by using one of the special needles devised by Kempton or Gardner and Murphy.

(*b*) Cutting-down method.—The internal saphenous vein at the ankle, a vein in the cubital fossa, or the cephalic vein at the wrist, are the most convenient. Any of these can usually be seen, or be made visible or palpable by compression of the limb proximally. Inspection and contemplation of the surface marking is recommended before the operation is begun. The internal saphenous vein will occasionally not have formed one stem at the site of election ; if a single venous trunk is not found, the other ankle or an upper limb vein must be chosen. The diameter of these veins in neonates is seldom much more than 1 to 2 mm. A Bateman needle, which has an inner cannula that can be removed and cleaned should it become blocked, is the cannula of choice.

Alternatively, a large sized hypodermic needle with the sharp end cut off and smoothed, a length of polythene tubing, or a small Hamilton Bailey intravenous cannula can be used.

Splinting the limb.—Satisfactory fixation of the cannula in the vein is of the utmost importance. Though immobile itself, it is important that the splinted part can be easily moved with the baby as a whole for nursing procedures such as changing the napkins, washing, feeding, and bringing up the wind. A baby in whom a drip transfusion is set up should not be considered an immovable object. The nursing movements of the baby are desirable in that they will help to prevent abdominal distension, œdema, infection in the naso-pharynx passing up the Eustachian tubes, and hypostatic pneumonia.

Fig. 663.—Splinting of Limb for Cubital Fossa Veins.

The splint should be light and lightly padded and long enough to extend from the knee or axilla to four to six inches beyond the end of the limb. The limb should be firmly but not tightly strapped to the splint. When

the ankle or wrist vein is used the foot or hand should also be strapped to the splint. Easy access for frequent examination of the proximal part is desirable so that excess bandages or other covering bound on to the limb is best avoided.

Cutting down and insertion of the cannula.

Instruments required :

1 2 c.cm. Record syringe (for local anæsthetic).
1 No. 20 hypodermic needle.
1 Catgut tube breaker.
1 Detachable scalpel blade No. 15 and No. 3 handle.
1 5-inch stitch scissors.
1 6-inch dissection forceps.
1 3-inch fine pointed dissection forceps.
1 small aneurysm needle.
Catgut 3/0 (for ligatures).
2 Spencer Wells' forceps.
2 Halsted's Mosquito forceps.
1 4-inch straight sharp pointed ophthalmic scissors.[1]
1 Bateman's needle.
No. 2 "Polythene cannula" (1 mm. internal diameter) about 9 inches.[2]
1 No. 4 curved cutting eye needle.
Ophthalmic silkworm gut (for skin sutures).

The surface marking of the internal saphenous vein is $\frac{1}{2}$ to $\frac{3}{4}$ inch above and medial to the tibial malleolus. Those in the cubital fossa or on the dorsum of the wrist can be seen. The skin is cleaned with an antiseptic solution. About 0·5 c.cm. of a local anæsthetic such as 1 per cent. procaine anæsthetizes the skin and subcutaneous tissue. The few minutes required for this to become effective can be usefully employed fitting the dripper and tubing to the flask or vacoliter containing the transfusion fluid, running the fluid through the tubing until air bubbles are excluded and ensuring that the cannula fits securely to the adaptor on the rubber tubing. Delay when the cannula is in the vein is thus avoided. A transverse incision about 1 cm. long is made through the skin at right angles over the line of the vein. The skin edges are separated by inserting closed artery forceps and opening them in the wound in the direction of the vein. If this is done several times the subcutaneous tissue will separate from the vein and the requisite half-inch will have been exposed by blunt dissection. The vein can be clearly verified by passing the forceps underneath deep to it and opening them again. A loop of fine catgut is drawn back (preferably size 000 gut). The loop is cut and the distal piece tied round the vein. The long ends from the knot are held in the artery forceps on which light tension will keep the vein taut and facilitate further manipulation. The anterior wall of the vein is picked up in fine mosquito artery forceps which remain in position until the cannula is safely inserted and tied into the vein. With fine, sharp-pointed scissors, reserved for this purpose and used for nothing else, a tiny snip is made in the vein immediately distal to the mosquito forceps. Care must be taken that the outer and inner walls of the vein are both cut. A hole in the vein is now held open by the mosquito forceps. The cannula, with stylet in position, is inserted and tied into the vein with the catgut just proximal to the forceps. The fluid from the flask is allowed to drip slowly through the inner cannula of the Bateman needle, or from the

[1] Messrs. John Weiss and Son, 287 Oxford Street, London, W.1.
[2] Messrs. Allen and Hanbury, Ltd., 48 Wigmore Street, London, W.1.

adaptor, and this is fitted firmly into the cannula in the vein. It is wise to allow a few cubic centimetres to run in quickly to ensure that all is well. To add to the safety of maintenance of the cannula in the correct position in the vein, a stitch is put through the skin distal to the incision and tied round the hilt of the outer needle.

The wound is sealed with a small square of gauze soaked in Whitehead's

Fig. 664.

Fig. 665.

Fig. 664 and 665.—Splinting of Limb for Wrist Vein.

varnish. Strips of strapping, one next to the adaptor, one over the tubing and two on to the splint a few inches beyond the limb, will fix the tubing so that it does not move the cannula in the vein and thereby damage the inner venous coat.

Polythene tubing.—This plastic tubing is obtainable with internal diameters of $\frac{1}{2}$ mm., 1 mm. and 2 mm. The 1 mm. size is the most convenient for general use, the $\frac{1}{2}$ mm. being too small for prolonged blood or plasma transfusions and the 2 mm. too big for most infant's veins. Although the tubing loses some of its flexibility on being boiled, this method of sterilization is satisfactory

providing it is carried out shortly before use and providing the tubing is only used once. After being boiled for fifteen minutes the tubing should be plunged into surgical spirit. Alternatively it may be cold sterilized for twenty-four hours in 1 per cent. cetrimide, the antiseptic completely filling the lumen of the tube.

A length of about 9 inches is cut. Into the proximal end (1 mm. tubing) is fitted the outer cannula of a Bateman's needle to act as a connector. The distal end is pointed with a pair of scissors. With skill it may be inserted into a vein the diameter of which appears to be one-third that of the tubing. It is then run up the vein for 4 or 5 inches and secured distal to the wound by a skin suture. 1 mm. polythene tubing may be inserted into a large vein by running it through a No. 13 S.W.G. needle. The use of polythene tubing complicates intravenous transfusion, but it has the great advantage that the child's limb

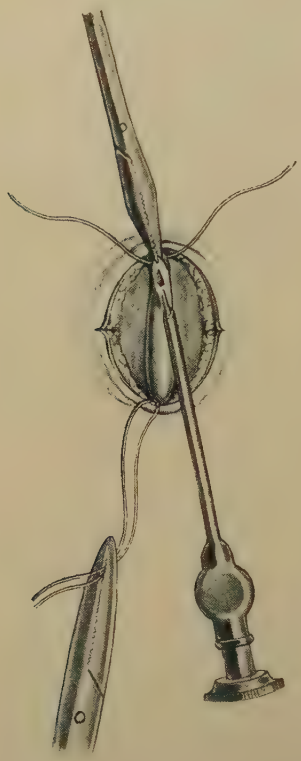


Fig. 666.—Mosquito Forceps holding up the Anterior Wall of the Vein so that the Needle may be surely inserted.

Fig. 667.

need not be completely immobilized, freer movement lessening the hazards of local œdema and infection (fig. 668).

Rate of flow.—This is controlled by a screw clip below the drip chamber. The desired rate per hour must be calculated rather than drops per minute, as the size of a drop can vary for many reasons; however, a sensible number of drops to start with is about 20 per minute with subsequent adjustment as necessary (this represents $1\frac{1}{2}$ to 2 ounces per hour). The reading from the flask or vacoliter should be taken every clock hour. Every case needs a carefully recorded chart of rate of flow, total intake by this and other routes, and estimated output by a note of urine, stools and vomits.

A vigilant watch must be kept on any patient in whom there is a drip transfusion in progress. Remarkable changes may occur in very short spaces of time. These patients should be visited by a doctor every few hours and the nursing staff trained to report anything untoward happening between times.

Once the initial dehydration has been combated, which in an infant

FIG. 668.—TO SHOW THE CONSIDERABLE FREEDOM OF MOVEMENT POSSIBLE WHEN A POLYTHENE CANNULA IS USED FOR INTRAVENOUS INFUSION.

of about 10 lb. will take some 3 to 4 oz. per hour for three to six hours, the formula $2\frac{1}{2}$ oz. per pound body-weight per day is a useful guide to the total fluid requirements of infants.

Size of transfusion of blood. A rough estimate of the volume in cubic centimetres of whole blood required to raise the hæmoglobin level to 100 per cent. (14·8 grammes per 100 c.cm.) may be calculated from the formula :

$$\frac{\text{Per cent. rise of Hb. required}}{\text{Per cent. Hb. of donor blood}} \times \text{Blood Volume}$$

The hæmoglobin concentration of depot blood varies considerably. When it is not practicable to estimate it directly it should be taken as 80 per cent. The blood volume is taken approximately at 77 c.cm. per kilo of body-weight (35 c.cm. per pound).

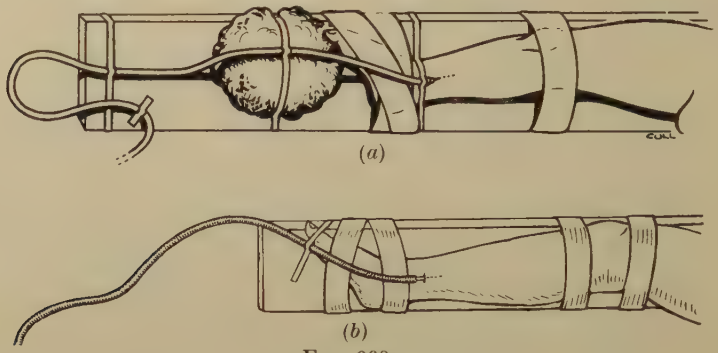


FIG. 669.

(*a*) The right way: showing the length of splint beyond the end of the limb to support the tubing firmly.
(*b*) The wrong way: no splint on which to fix tubing which can therefore move the needle considerably and thus damage the vein.

Complications:

Spasm of the vein is likely in excessively dehydrated or shocked infants or if the procedure of cannulizing the vein has been unfortunately prolonged. Spasm should not last longer than ten to fifteen minutes and will be overcome by keeping the infant warm with electric pads or bottles and blankets and by raising the flask on a pole as much as six to eight feet above the level of the vein. The spasm of the vein will prevent an immediate fast flow when first the adaptor is connected with the needle. When the spasm is relieved the fluid will rush in unless a close watch is kept during the first few minutes and the screw clip tightened.

THE HOSPITAL FOR SICK CHILDREN

INTRAVENOUS DAILY FLUID CHART

Name.....*Birth Weight*.....*Present Weight*.....*Date*.....

Time	Reading on Scale of Bottle	Amount in Hour	Rate of Drip	Total of To-day	Remarks	Fluids by Mouths	Vomits	Stools	Urine
A.M.									
0									
1									
2									

Total fluid for the day, in ounces =

FIG. 670.—SPECIMEN CHART FOR RECORDING FLUID INTAKE AND OUTPUT.

Tight binding proximally may so compress the tissues that the venous return from the limb is prevented and then the drip will not run. Binding which has not at first been too tight may become so with the improved hydration of the tissues or movement of the limb from bad splinting or from localized œdema, which not infrequently occurs after a transfusion has been running for several days.

The outer venous coat can fairly easily be separated from the inner even in the smallest vein, therefore it alone may be picked up in error in the mosquito forceps and when the scissor cut is made the venous channel is not opened. The needle then passes up between the outer and inner coats. Experience will show, however, that considerable resistance is met when this occurs whereas if the lumen of the vein has been satisfactorily entered the needle is pushed in without difficulty.

Kinking of the vein by the needle lying in an unnatural position in its course is rectified by adjustment of the direction of the needle.

Overloading the system with fluid should not occur providing continual check is kept on the rate of drip. The clinical condition of the infant has to be constantly reassessed with particular reference to possible commencing œdema.

Sepsis leading to thrombo-phlebitis may occur. The frequency is directly proportional to the amount of interference during the course of the continuous drip. The dressing over the incision and cannula should be treated with as much respect as that covering any operation wound ; it is desirable to leave it *in situ* and not to meddle. If adjustment becomes imperative strict aseptic precautions must be enforced. A smoothly running continuous drip transfusion may run for many days without becoming infected. The longest time the writers have seen a drip running in one vein in an infant is eleven days.

It is best to stop the transfusion at the first sign of thrombo-phlebitis or lymphangitis, but occasionally an infant's life may depend on the continuance of the transfusion. Therefore, the nursing staff should be instructed that, should signs of local infection appear, the doctor must be consulted as to the advisability of stopping the transfusion. With suitable chemotherapy the inflammation can usually be checked and as a rule clears up rapidly on completing the transfusion and removing the cannula.

In the event of the drip ceasing ascertain that :

(*a*) the baby is warm ;
(*b*) the tube is not kinked ;
(*c*) pressure along the line of the vein has not occurred ;
(*d*) the cannula is in the optimum position with reference to the vein ;
(*e*) increased head of pressure by raising the height of the flask has been tried ;
(*f*) the patency of the needle is satisfactory. Without moving the dressing over the wound the inner needle can be withdrawn and syringed through, or the outer needle can be tested by syringing through $\frac{1}{2}$ c.cm. normal saline.

Rapid Intravenous Transfusion

Drip transfusion is unnecessary if only small volumes of blood are needed as, for instance, in mild anæmias due to infection in infancy or for repeated transfusions in erythroblastosis fœtalis.

Blood, not exceeding 10 c.cm. per pound body weight, may be injected over a period of about half an hour using the technique described below. Larger volumes should not be used, nor should the transfusion be more rapid, for fear of overloading the circulation. The scalp veins provide the most convenient site for injection in infants, but veins on the back or front of the wrist, in the antecubital fossa or occasionally the external jugular may also be used.

Fig. 671. General View of Scalp Vein Injection.

The procedure can be repeated as often as eight to twelve hourly if necessary, even into the same vein.

Procedure.—Scalp vein injection. One of the branches of the temporal vein will usually be found most convenient; alternatives are the post-auricular and the frontals. The head must be shaved over the chosen veins. The veins are only easily distinguished from the arteries by palpation of the beat in the latter. Good team work is essential: one assistant must hold the baby correctly with the head perfectly still; another assistant must work the three-way tap; while the operator inserts the needle.

The baby is wrapped with its arms firmly immobilized in a blanket. The head is held in the finger-tips of both hands, one thumb able to compress the vein just anterior to the pinna, the other over the mastoid process, the forearms grasping the trunk of the baby to prevent wriggling. The best position for the baby is transversely across the cot or operating table with the top of the head level with the edge. The operator sits down and must be in a sufficiently comfortable position to be able to hold the needle in the vein securely during the injection of the fluid. A Kaufman syringe is used, preferably all glass and with a longitudinal groove along the plunger. The needles (Luer fitting) are short bevelled, about half an inch long, of sizes 20 to 24 S.W.G. There is a safety chain between the plunger and syringe which prevents the plunger being pushed out during injection. About 100 c.cm. of sterile normal saline is poured into the reservoir and by alternately filling and emptying the 20 c.cm. two-way syringe the entire system is freed from air bubbles. The saline is then ejected until its level reaches the neck of the reservoir, which is then filled with 100 to 150 c.cm. of blood. The 20 c.cm. syringe is again filled and emptied via the Kaufman syringe until the system contains more or less undiluted blood.

The best vein is chosen and made to stand out by compression proximally and a gentle tap over its length. No local anæsthetic is used. The needle is

most reliably inserted by piercing the skin just next to the vein and then moving the needle over the vein before entering the lumen. A slight threading motion will help to keep the needle in the lumen. Negative pressure by constant attempts at withdrawal of the Kaufman syringe plunger will usually be necessary to decide when the vein has been entered; sometimes the pressure of blood in the vein is sufficient to push the plunger back. When blood is obtained the plunger is withdrawn past the side arm (this is facilitated by rotating the plunger until its groove lies opposite the side arm), the compressing thumb of the assistant is released, and the blood is injected by the assistant in charge of the three-way tap.

Fig. 672.—Scalp Vein Injection.

If the baby moves, or for any other reason the needle unfortunately slips out of the vein, a subcutaneous bleb of fluid will immediately be seen; also there is at once a sudden increase of resistance to the injection. It is not possible to re-enter the same vein at once, which must be abandoned until bleeding from the puncture has ceased. The vein will, however, recover and be ready for use again if necessary in a few hours' time.

The annoyance of tubing slipping off the various connections will be obviated by thread ties.

Chamberlain's modified all glass Kaufman's syringe (No. K606YC) may be obtained from Messrs. Becton, Dickinson and Co., Rutherford, N.J., U.S.A.

Bone Marrow Infusion

This route may be found useful in the following circumstances:

(i) Babies in whom the veins in the usual sites have been used yet still require parenteral fluid.

(ii) Shocked and premature infants in whom a minimum of disturbance is desirable.

(iii) Patients in whom repeated blood transfusions have been given, or will be required, as in hæmophilia and aplastic anæmias.

The bone marrow of the tibia is the site elected. The marrow cavity in the sternum of infants, and in fact considerably older children, is not large enough for this to be a practicable place for the reception of transfusion agents.

Procedure.—The Gimson needle is recommended.

The flat subcutaneous plate of bone on the tibia inferior and medial to the anterior tibial tuberosity is palpated. The limb is splinted in a semi-externally rotated position as for cutting down on to the internal saphenous

vein at the ankle. The skin is cleaned. A non-touch technique is maintained so far as is possible as during any operation involving bone. A local anæsthetic impregnates the skin subcutaneous tissue and periosteum. The needle and stylet, with the handle attached, are taken and, with the needle at right angles to the plate of bone *i.e.* pointing postero-laterally with reference to the leg itself—are inserted with a firm twisting motion as when using a bradawl. The needle passes through the cortical bone with a crisp crunch. The flange rests lightly on the skin. When the stylet is withdrawn a small

FIG. 673.—SHOWING THE SIZES OF NEEDLES WITH THEIR OWN STYLETS, THE ADAPTOR AND HANDLE.

amount of marrow may well up or be sucked up into a syringe ; it seldom flows out freely. The adaptor, filled with the infusion fluid and attached to the tubing from the dripper and bottle, which has already had air bubbles excluded, is fitted to the needle and the flow started.

Any of the usual infusion fluids may be given in this way : saline, Hartmann's solution, blood, serum or plasma.

The older the child the larger the marrow cavity and therefore the faster the flow can be. In a neonate a rate of more than half an ounce an hour is seldom obtained. Whereas in a child of six months, particularly if dehydrated, a rate of 2 or 3 oz. an hour can usually be expected. It will not infrequently be found that a sufficiently rapid rate of flow is only obtained by raising the

flask some six to eight feet above the level of the limb. The longest time the writers have seen one bone marrow infusion maintained was six days; it was then only discontinued as the baby required no more parenteral fluid.

Particular attention should be paid to the following points:

(i) Emphasis is laid on the necessity for inserting the needle at right angles to the surface of the tibia.

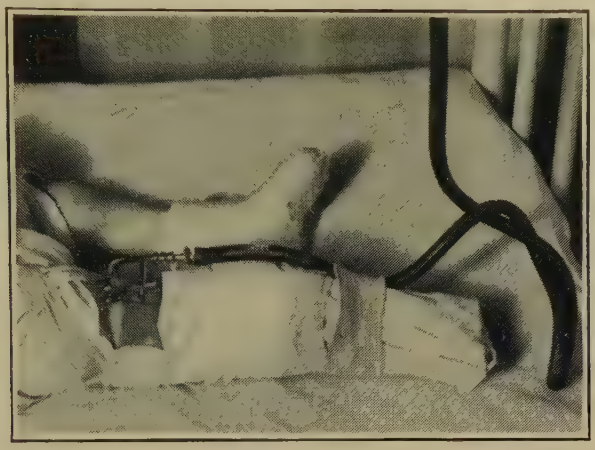
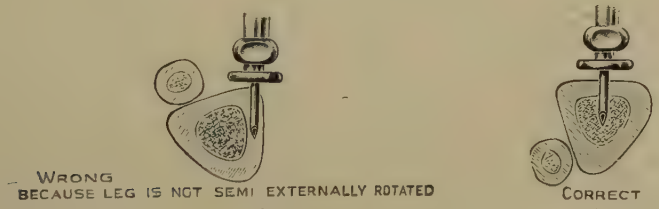


Fig. 674.—Tibial Transfusion in a Boy 3 Months old.

This is facilitated by the position of semi-external rotation of the limb. Fig. 675 shows the error of attempting to insert the needle in the antero-posterior direction of the limb, as might happen if the leg were not splinted in the correct position. It is wise to inject a small amount of saline through the needle as soon as it has been inserted to ensure that the marrow has been entered satisfactorily.

(ii) If the needle works loose, fluid will leak back into the subcutaneous



(*a*) (*b*)

Fig. 675.

tissues and the limb will become œdematous; the transfusion must then be stopped. A careful watch for œdema should be kept during the first hour or two of the transfusion, because if œdema is allowed to develop a pressure necrosis of the skin beneath the flange might result.

(iii) Dislodging by kicking with the other leg is prevented by anchoring it with a bandage noose round the ankle. A small cradle will prevent disturbance by the bed-clothes.

(iv) Osteomyelitis is the danger which should not be forgotten. The immediate emergency of the patient's condition justifies the problematical risk of infection. Penicillin added to the fluid will largely prevent this.

(v) If a second transfusion is required, soon after the first has been discontinued, the other tibia must of course be employed, as leakage back through the original hole will make that leg useless for the purpose.

Subcutaneous Fluids

Mild degrees of dehydration can satisfactorily be combated by this route. It is useful before operation for pyloric stenosis or for mild cases of gastro-enteritis. Normal saline or half normal saline with 5 per cent. dextrose may be used, although dextrose solutions do sometimes cause mild inflammatory reactions. Absorption from subcutaneous tissues can be greatly accelerated by the simultaneous local administration of hyaluronidase. However, this is not a satisfactory substitute for intravenous drip transfusion in the severely dehydrated infant as (1) the site of the injection has to be changed at inconveniently frequent intervals for prolonged transfusion, (2) the control of the fluid intake is less reliable and (3) occasionally a widespread subcutaneous œdema develops without the generalized dehydration being relieved.

Direct injection or continuous drip are effective. Continuous drip allows an ounce or two more but takes a longer time and involves perhaps rather more discomfort, though it is less immediately exhausting to the infant.

The sites of choice will be the outer aspect of the thighs, the anterior axillary and sub-pectoral regions, or the lower scapular areas. The site of injection will have to be changed every twelve to sixteen hours.

Direct injection requires gentle massage for the ten to fifteen minutes afterwards to aid absorption. Two or three ounces each side will generally be absorbed.

Procedure of subcutaneous drip.—The flask and dripper are attached to the two needles by tubes and ⅄-connection. Special subcutaneous needles (20 S.W.G. 1½ in.) or intramuscular needles (No. 12 hypodermic gauge or No. 1 if larger bore is required) are suitable. A screw clip is attached to the tube from each needle. Fluid is run through and air excluded. The needles are inserted subcutaneously and maintained in position by strapping across the hilt. A pad of warm wool is placed over the part. One milligram of hyaluronidase powder dissolved in 1 c.cm. of sterile water is then injected into the rubber tubing near its attachment to the needle. The hyaluronidase injection must be repeated

Fig. 676.—Subcutaneous Saline.

after eight hours. The rate of drip can usually be maintained at about 1½ ounces an hour.

Reactions occasionally occur in the form of a transient rise of temperature during the following six to twenty-four hours.

Intramuscular Drip Fluid Administration

Saline may be given by the intramuscular route as an alternative to the subcutaneous. Depending on the size of the child and the degree of dehydration, 12 to 20 oz. in twenty-four hours may be expected as total for both sides. The sudden stretching of muscle by a large injection is painful, but by the drip method normal saline is well absorbed painlessly.

The method is simple and the same apparatus is used as for the subcutaneous drip. Hypodermic needles are quite adequate, or special intramuscular needles can be obtained. The site of choice is the outer aspect of the thighs, as for intramuscular injections. The needles, one into each side, are inserted at right angles to the skin until the femur is just touched, they are then withdrawn ⅛ to ¼ inch and strapped *in situ*.

Rectal Fluid

This route of fluid administration, of tap water, saline solution, or dextrose solution (6 per cent.), is practicable in children over about five years of age, used in the same way as for adults. In infants and younger children the passage of the catheter induces straining and the fluid is not retained. It is more often used for surgical cases than for medical, for instance during the immediate post-operative period before fluids can be taken by mouth, since the medical dehydration problems are so frequently associated with diarrhœa.

Exchange Blood Transfusion through the Umbilical Vein

Although exchange transfusion has been used as a treatment for leukæmia, its main application is in cases of erythroblastosis fœtalis. The procedure is best carried out as soon as possible after birth and the umbilical vein then provides the most convenient channel for the exchange. The indications for replacement of the infant's blood are described on page 1071.

The apparatus required is shown in fig. 677. The 1 mm. diameter polythene tubing is best connected to the distal three-way tap by means of a type of ureteric catheter adaptor (as illustrated) which makes a leak-proof joint by the pressure of a rubber diaphragm on the *outside* of the cannula. With this adaptor there is little risk of blood clotting at this junction.

Essentially the procedure consists in withdrawing 20 c.cm. of the infant's blood and replacing with 20 c.cm. of fresh compatible Rh-negative blood and repeating withdrawal and injection alternately until approximately 90 per cent. of the baby's blood has been exchanged. The aim should be to leave a final hæmatrocrit of 50 per cent., only 5 per cent. being the infant's cells and 45 per cent. Rh-negative cells. To produce a

final hæmatocrit of 50 per cent. on the basis of a simple exchange of blood it is clear that packed cells must be used, as the hæmatocrit of unconcentrated donor blood seldom exceeds 35 per cent. If only unconcentrated blood is available the hæmatocrit can be raised to 50 per cent. by giving a final additional transfusion after the exchange. This is permissible, if the baby is in good condition, without clinical evidence of cardiac failure and with a normal venous blood pressure. If, however, the baby's condition is poor no final additional transfusion should be given. The main objective, that of removing 90 per cent. of the infant's red cells and plasma, will have been achieved by the exchange, but unless packed cells have been

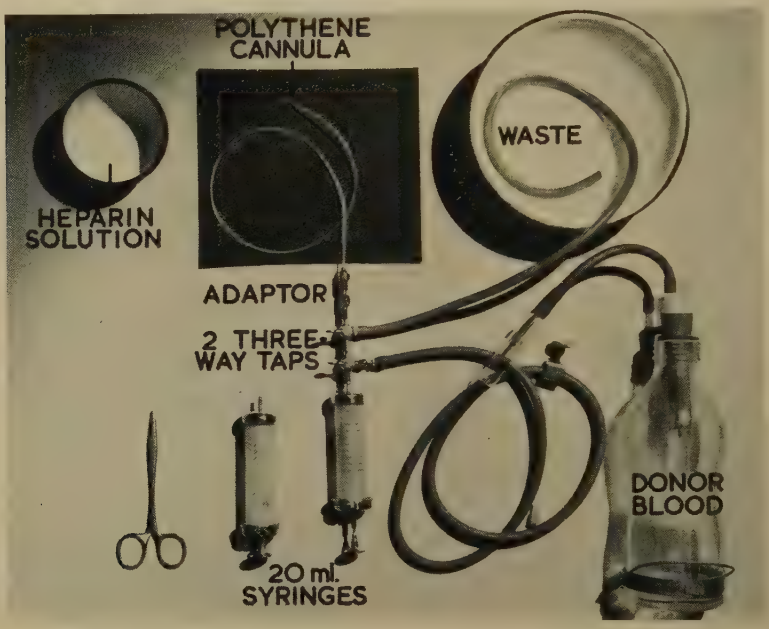


Fig. 677.—Apparatus required for Exchange Transfusion.

used, it may be necessary to give small transfusions by scalp vein injection in the course of the next few weeks to correct the mild anæmia.

The quantity of blood that must be exchanged and the size of any additional transfusion needed depend on the baby's blood volume (calculated from the birth weight) and the packed cell volumes of the baby's venous blood and of the donor's blood. The answer can be most rapidly and conveniently determined by use of the nomogram prepared by Veall and Mollison (fig. 678).

Procedure.—This can usually be carried out up to twenty-four hours of age. The infant should be left in the cot and kept warm. The umbilical cord is cut about $\frac{1}{2}$ inch from the skin. The large thin-walled vein is easily distinguishable from the two small thick-walled arteries. Polythene tubing (1 mm. in internal diameter) is introduced into the vein for about one inch and an attempt should then be made to remove any blood clot present by gently withdrawing the tubing while a negative pressure is maintained within it by the syringe. The

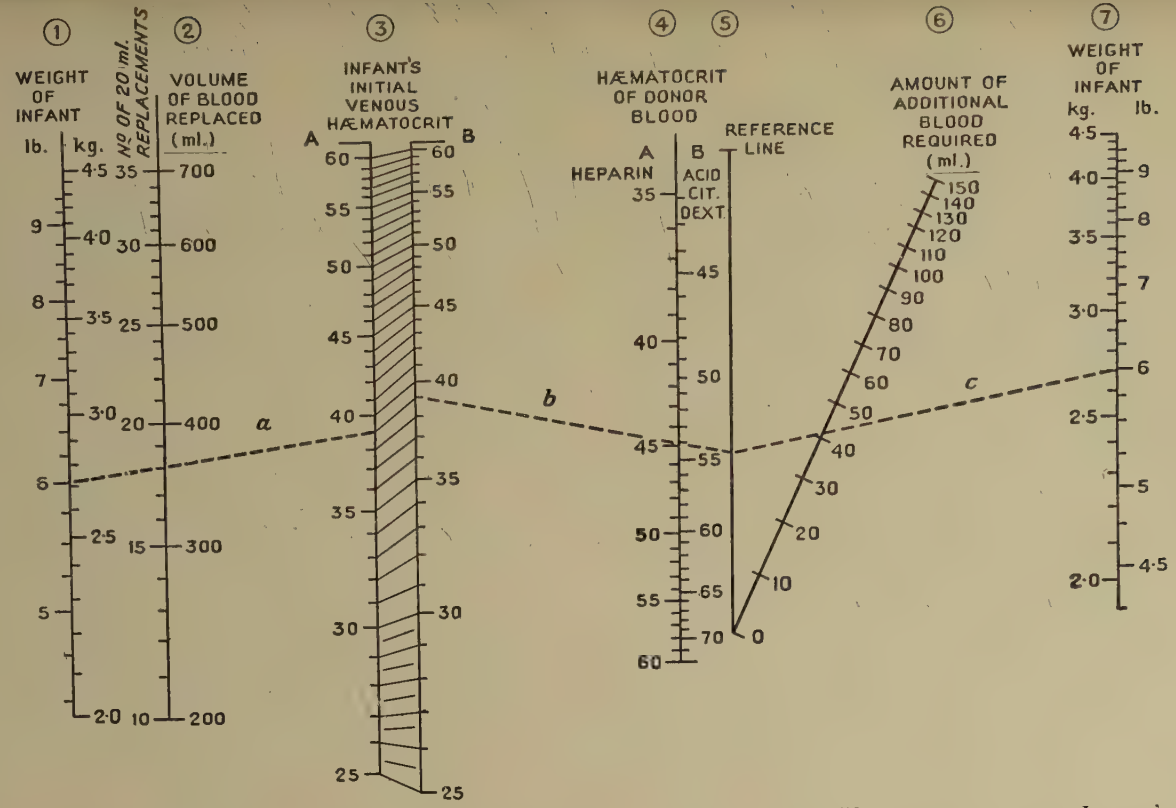


FIG. 678.—NOMOGRAMS FOR REPLACEMENT TRANSFUSIONS, TO REDUCE THE HÆMATOCRIT OF THE INFANT'S OWN RED CELLS TO 5 PER CENT. AND TO LEAVE THE INFANT WITH A FINAL HÆMATOCRIT OF 50 PER CENT.

The volume of blood to be exchanged can be read from column 2, by joining the appropriate points on columns 1 and 3. The volume of the final additional transfusion (if given) can be read from column 6, by joining the appropriate points on columns 3 and 4, extending the line to column 5 and joining this point to column 7. The dotted line shows an example.

Note that by using a concentrated red-cell suspension, the injection of additional blood at the end of the

tubing is then reinserted and pushed gently into the vein for two or three inches until venous blood can readily be withdrawn. It is important to cut the end of the tubing transversely and not to make a bevel as a sharp tip may pierce the wall of the vein. Some difficulty may be experienced in introducing the cannula, but this can be overcome by gently pulling the stump of the umbilical cord outwards and downwards whilst cautiously pushing the tubing onwards.

Blood is then withdrawn from the infant into the 20 c.cm. syringe and expelled into the waste basin. (In withdrawing blood the plunger of the syringe should not be pulled back too forcibly, as this may result in a cessation of the flow presumably due to collapse of the vein.) By turning the taps the syringe is then filled with donor blood which is injected into the infant. The polythene tubing should be watched carefully to detect and prevent accidental infusion of air bubbles. It is best to warm the donor blood but great care should be taken that the temperature of the water bath in which it is warmed is not above blood heat. From time to time the syringes, taps and waste tube should be washed out with heparin solution (1,000 units in 100 c.cm. of sterile saline solution), but none should be allowed to enter the infant's circulation. If whole citrated blood is used 1 c.cm. of 10 per cent. calcium gluconate solution should be injected slowly to prevent tetany after each 100 c.cm. has been exchanged.

It is wise to measure the venous blood pressure at intervals during transfusion. The polythene tubing adaptor is disconnected from the three-way tap and raised so that the height of the column of blood may be measured against a sterile 10 cm. steel ruler placed just above the umbilicus (Diamond *et al.*, 1951). If the pressure is above the normal of 6 cm. or if there is clinical evidence of heart failure, more blood is withdrawn than injected until the normal venous pressure is restored.

The procedure is usually completed after, say, 400 c.cm. have been exchanged (fig. 678, column 2), when, if necessary and safe, the final injection is given slowly (fig. 678, column 6). The cannula is then removed and the umbilical stump ligated.

If attempted exchange transfusion is unsuccessful it is often possible to give a drip transfusion through the umbilical vein using the polythene cannula.

Withdrawal of Blood

A prick of the finger or heel will provide 1 c.cm. of blood if the correct technique is used. The finger or foot should be held as shown in fig. 679 and 680 and a single prick made with a Hagedorn's needle or preferably with a glass pricker (fig. 681). If serum is required the blood is best collected in a Lyon's tube (fig. 679 and 680) or in a Wright's capsule ; if unclotted blood is required it should be run into a bijou glass bottle containing the necessary anti-coagulant. It is important to allow the blood to run down the same channel in the glass until sufficient is collected and to agitate the bottle frequently to ensure mixing the blood and the anti-coagulant. Alternate gentle squeezing (not permissible for blood counts) and relaxation will accelerate the flow of blood, as will prior immersion of the limb in warm water.

When more than 1 c.cm. of blood is required a venepuncture will be necessary. It is difficult to obtain blood from a vein of the cubital fossa from children under three to five years : this of course depends on each individual case ; therefore it is always worth examining these veins before trying elsewhere. However, various other possibilities present themselves :

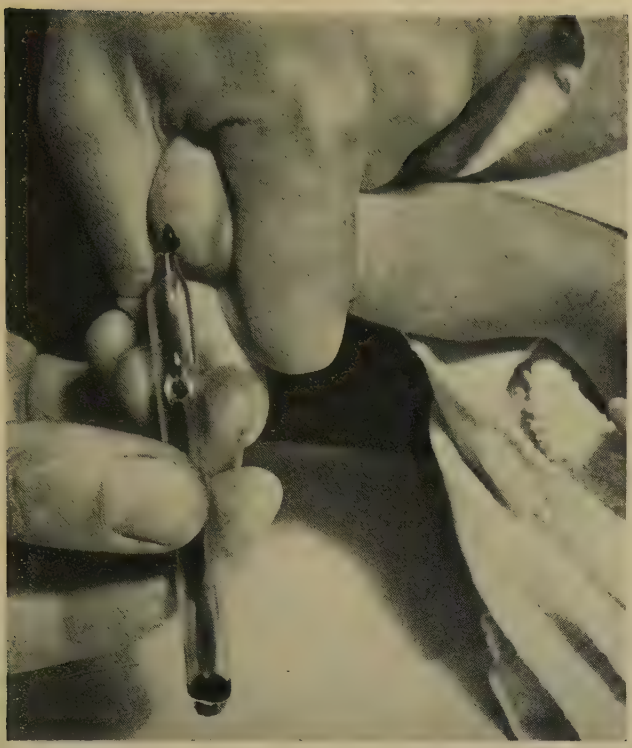


FIG. 679.—COLLECTING BLOOD FROM A HEEL PRICK INTO A LYON'S BLOOD TUBE.

Note that the narrow part of the tube has been broken off and that the side hole is opposite the stream of blood.

FIG. 680.—COLLECTING BLOOD FROM A FINGER PRICK INTO A BIJOU BOTTLE.

the external jugular, the internal jugular, the femoral, a scalp vein and the anterior fontanelle.

In all these cases the way in which the child is held will be of the utmost importance and will make a great difference to the ease of the procedure.

(i) **The external jugular.**—This vein is easily seen as it crosses the sterno-mastoid muscle when the baby cries and when the vein is compressed proximally. Perhaps therefore this is the one case in which it is better not to have too contented a child. The difficulty of this vein is its extreme mobility; there is little in the subcutaneous tissue anchoring it and the sterno-mastoid muscle does not form a firm backing, hence the vein easily slips aside.

FIG. 681.—A LYON'S BLOOD TUBE AND A WRIGHT'S SILVER PRICKER.

The former is easy to make, the latter requires some skill. For details see references.

The baby is held supine firmly wrapped, the head rotated facing over its opposite shoulder from the vein chosen. It will generally be easiest to enter the vein where it lies on the sterno-mastoid muscle. It makes little difference whether the needle points up towards the jaw or down towards the clavicle.

FIG. 682.—INTERNAL JUGULAR VEIN PUNCTURE.

When the necessary amount of blood has been obtained the needle is withdrawn and firm pressure applied to the puncture site while the patient is held sitting up. Thus a hæmatoma is prevented and the vein can be used again.

(ii) **The internal jugular.**—Here the binding of the patient in the blanket must allow full exposure of the supra-sternal notch. The child lies on its back with the shoulders above the top of the blanket; the left

edge is bound over the right arm and under the body, the right edge over the left arm and tightly across the chest diagonally and pinned under the right arm and body. The baby is placed across a firm surface so that the head hangs over the edge. The head is turned at right angles facing away from the side of internal jugular chosen (usually the right so the head is rotated to the left). The neck is fully extended. The operator will find it most comfortable to sit down. The left forefinger is placed in the supra-sternal notch. The needle on the syringe is then inserted at the mid-point of the posterior border of the sterno-mastoid and directed upwards and medially towards the tip of the finger which is denoting supra-sternal notch. Frequent withdrawal of the plunger of the syringe is advisable until blood is obtained. As soon as the needle is withdrawn the child should be sat up.

This perhaps sounds alarming, but in practice it is most efficacious. It is an excellent site from which to take blood for blood culture since any amount can be obtained.

There are, however, three serious dangers of which the operator should be aware before embarking on this procedure. Each can be avoided by reasonable care.

(1) Air embolism. The needle must fit securely on to the syringe and the plunger should be pushed down to expel all air from the barrel before the injection is made.

(2) Puncture of the trachea. Two fatal cases of interstitial and mediastinal emphysema have been reported following this mishap (Goldstein, 1949). It should be avoided by directing the needle as superficially as possible behind the sterno-mastoid.

(3) Hæmatoma formation. Blood from a punctured jugular vein may seep down behind the deep cervical fascia into the mediastinum. Hæmorrhage from the jugular is very unlikely except where a bleeding tendency exists. This procedure should, therefore, be avoided in icterus gravis neonatorum and hæmorrhagic diseases.

(iii) **The femoral vein.**—The point at which this vein is punctured is immediately distal to the inguinal ligament. Here it occupies the

FIG. 683.—FEMORAL VEIN PUNCTURE.

middle compartment of the femoral sheath and is *medial* to the artery. The artery separates it from the femoral nerve.

The baby is placed lying on its back across the cot with the hips slightly extended by the buttocks being on a sandbag. A nurse stands at the head with her arms on the baby's arms and her hands firmly holding the buttocks on the sandbag. If possible, another assistant holds the legs down, most conveniently just over the edge of the cot. The right femoral vein is the easier for a right-handed operator, since while the left fore-finger palpates and covers the femoral artery the right hand is free to direct the needle into the vein as it lies medial to the artery.

This method of venepuncture is satisfactory for taking blood for blood culture; as from the internal jugular any amount of blood can be obtained.

(iv) In skilled hands a **scalp vein** will yield 2 or 3 c.cm. of blood provided a really close-fitting syringe and a sharp short-bevelled needle are used.

(v) **The anterior fontanelle.**—Owing to the danger of intracranial hæmorrhage this route should not be used by the inexpert, nor until other possibilities have been exhausted. The skin must be shaved over the fontanelle and for an area half an inch all round. The baby is firmly wrapped in a blanket so that the arms are immobilized. The baby is best placed lying on its right side diagonally across the cot or table with the top of the head pointing to the operator's left shoulder. The needle should be short bevelled. It is inserted a quarter to half an inch in front of the posterior angle of the fontanelle in the mid-line and at an angle of 30° with the head surface. Blood is withdrawn from the superior sagittal sinus. Care must be taken not to pierce the inner wall of the sinus.

N.B.—It might here be mentioned that though blood may be withdrawn from the superior longitudinal sinus no fluid should ever be given this way. The cut-down technique cannot here be employed so that of necessity a sharp needle would be used; the slightest movement of this needle in the vein might cause damage or perforation of the wall with consequent thrombosis or hæmorrhage; further there is always the danger of sepsis. Such a procedure cannot be too strongly deprecated.

Bone marrow

Red marrow is best obtained from the upper end of the tibia in infants and from the ilium or sternum in children over 1 year of age.

1. Tibial Puncture.—A Gimson needle is inserted as described in the section on marrow transfusion. A 20 c.cm. syringe is then fitted and the plunger sharply withdrawn. As soon as any red marrow is observed entering the barrel of the syringe, both syringe and needle are withdrawn. Continued negative pressure may cause the marrow sample to be mixed with blood, whereas the contents of the needle are sufficient for biopsy and several smears (see page 1052).

2. Sternal Puncture.—A Waterfield needle [1] and handle is the best instrument for this procedure as the screw thread prevents the guard from slipping and reduces the risk of piercing the posterior table (fig. 684). The child should be quietened by giving a sedative three-quarters of an hour before the operation

[1] The "Modified Waterfield's bone marrow puncture needle" may be obtained from Messrs. S. J. Owen, 35 Northampton Square, London, E.C.1.

(nembutal grains ½ per stone of body weight). The child should be wrapped in a blanket so that his arms are held securely to his sides, the upper edge of the blanket just covering the lower end of the sternum. A small sandbag is placed between the scapulæ. The site of the proposed puncture is then indicated by marking the skin with horizontal lines in the centre of each second intercostal space near the sternal edge and with vertical lines in the

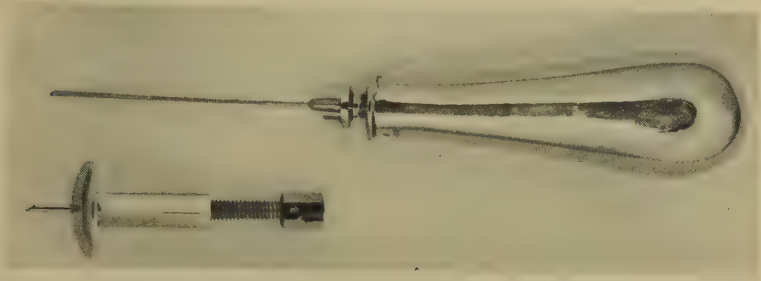


FIG. 684.—WATERFIELD'S MARROW PUNCTURE NEEDLE.
(Note the guard on a screw thread.)

centre of the sternum above and below the site of puncture. Thereafter a "no touch" technique should be employed. The skin is cleaned with cetrimide and ether. An intradermal bleb of 2 per cent. procaine is made at the site of the puncture and the periosteum is then infiltrated with about 1 c.cm. of the local anæsthetic. The guard on the Waterfield marrow needle is adjusted so that the tip of the needle protrudes about $\frac{3}{16}$ inch. The needle and holder are then held vertically and introduced into the bone with a screwing motion. A crunching sensation will be felt as the needle passes through the outer table of the bone. If this does not occur the needle should be withdrawn and the guard screwed a little further back. Once through the outer table the needle is removed, a 20 c.cm. syringe affixed and marrow withdrawn as described above. It is usually easy to tell if the tip of the needle is within the marrow cavity as in these circumstances the withdrawal of the plunger causes pain.

FIG. 685.—THE ILIAC CREST GRIPPED BETWEEN FINGER AND THUMB.

3. ILIAC PUNCTURE.—Iliac crest puncture is both less alarming to the child and easier to perform than sternal puncture. The ilium usually contains red marrow up to the age of puberty.

The guard on the Waterfield needle is screwed back until ½ to ¾ inch of needle protrudes. A Sahli's needle is also satisfactory. Then, after skin preparation and local anæsthesia, the puncture is made through the crest of the ilium one or two inches posterior to the anterior superior iliac spine in the plane of the ilium, so that the needle passes between the outer and inner laminæ. The distance the needle is

introduced into the marrow cavity need not, in contrast to sternal puncture, cause concern. The rest of the operation is carried out as described above. (See fig. 685–687).

FIG. 686.—THE WATERFIELD NEEDLE INTRODUCED.
(Taken from the child's right side.)

FIG. 687.—THE HANDLE IS REMOVED AND A 20 C.CM. SYRINGE IS FITTED.
The plunger is then withdrawn. The operator's left hand is seen gripping both syringe and needle, ready to remove both together, when red marrow first appears in the barrel.

Collection of Urine

This procedure is so essential, but so curiously seldom performed, that it is difficult to lay sufficient emphasis on its value. Countless times the illness of an infant could be accounted for and treated at the outset if only a specimen of urine had been obtained and examined microscopically —the urinary infection would be revealed.

Females.—Catheterization is performed with the infant lying on her back, the buttocks over a sandbag, most easily with an assistant

standing at the head of the patient holding the legs as fully flexed as possible. The labia are separated and cleaned with 1 in 2,000 mercuric chloride solution, a fresh swab for each cleansing sweep from before backwards. The urethral orifice is identified and a sterile rubber catheter (no. 3), lubricated with glycerine, inserted. The urine is allowed to flow into a sterile test tube and a drop should be examined at once under the microscope, before the specimen is sent to the laboratory.

Males.—It is seldom necessary to catheterize a boy as the collection of a clean specimen is comparatively easy. The foreskin and glans are

FIG. 688.—COLLECTION OF URINE.

swabbed with 1 in 2,000 mercuric chloride solution. The penis of the infant is then fitted into a sterile test tube which is kept in position with strapping.

Alternatively a sterile finger cot is easily applied. It is never long before a specimen is obtained.

Cerebro-spinal Fluid

(i) **Lumbar puncture.**—The position of the child, as for the adult, is either lying on the left side or sitting, and the procedure is similar to that for an adult, though a shorter needle with smaller bore is more suitable (Bier's needle, or Pannett's needle 18 to 20 S.W.G., 2 to 3 inches long). General anæsthesia may be necessary for children over one year or until they are old enough to be cajoled into co-operating.

It is important that the assistant holds the child immobile with the spinal column flexed and the vertebral bodies in a straight line with no

scoliosis or rotation. The space chosen is usually between the third and fourth lumbar spines (the fourth is level with the iliac crest). The spaces between the second and third, or the fourth and fifth, may be used, but the former should be avoided in infants as the cord may be damaged. The theca is highly vulnerable to infection. Strict asepsis must be employed and all the instruments must be dry-sterilized. The sensation of penetrating the ligamentum flavum is less definite in a child than in an adult so that frequent withdrawal of the stylet is advisable. Measurement of cerebrospinal fluid pressure may not be reliable in infants as such wide variations occur with apparently little disturbance; crying, holding the breath, sudden rapid respirations, pressure on the abdomen, all raise the pressure. Lumbar puncture should not be carried out when the presence of a cerebral tumour is suspected, owing to the risk of producing a pressure cone in the foramen magnum.

INSTRUMENTS REQUIRED:

6-inch dissection forceps (for skin preparation).
2 c.cm. Record syringe (for local anæsthetic).
No. 20 hypodermic needle.
Pannett's or Howard Jones' spinal needle, 18 to 20 S.W.G., 2 to 3 inches long.
Tubing adaptor (Record fitting).
Greenfield's spinal manometer.

(ii) **Cisternal puncture.**—With care this need not be considered a dangerous procedure. It is one in which confidence may be developed from practice on the cadaver. It is useful in cases of suspected spinal block or when a blood-contaminated specimen has unfortunately been obtained from lumbar puncture, or when lumbar puncture has failed.

Again it is important that the assistant holds the child immobile in the correct position. The child lies on the left side; the head is flexed forward with the sagittal suture, base of occiput and seventh cervical spine in line, and the natural cervical lordosis obliterated. The hair must be shaved over the base of the occipital bone. The impression between the base of the occipital bone and the posterior tubercle of the atlas is palpated. The needle is inserted in the midline through this space. The cisterna magna (cisterna cerebellomedullaris) will usually be entered when the needle is pointing in the line of the nasion, or lower eyelid. However, it is safest to feel along the base of the occiput by gently touching the bone, withdrawing the needle, inserting a little farther along and so on until the subarachnoid cavity is entered. The circumference of the neck divided by eight or nine is a good estimate of the depth of tissue which has to be pierced before the cistern is entered.

(iii) **Lateral ventricular puncture.**

INDICATIONS:

Diagnosis.—(1) Examination of the cerebro-spinal fluid where a spinal or basal subarchnoid block exists or in cases of suspected cerebral tumour.
(2) For air ventriculography.
(3) For dye studies in cases of hydrocephalus.

Therapy.—For the reduction of intracranial pressure or the introduction

of drugs into the cerebro-spinal fluid in cases of tuberculous meningitis or in purulent meningitis with spinal or basal block.

In infants access may be obtained via the anterior fontanelle; in older children a burr hole will have to be made in the skull.

Technique.—The whole scalp must be shaved and the skin prepared. The infant, securely wrapped in a blanket, lies supine and the head is held firmly by an assistant. A lumbar puncture needle may be used but there is an undoubted risk of its piercing a blood vessel in its passage through the brain and it is preferable to employ a fine brain cannula [1] (see fig. 689). With the aid of a sharp trochar the cannula is introduced at the lateral angle of the fontanelle 2 cm. from the midline to avoid the sagittal sinus. When the skin and dura have been penetrated the trochar is replaced by a blunt stylet and the cannula is directed downwards and

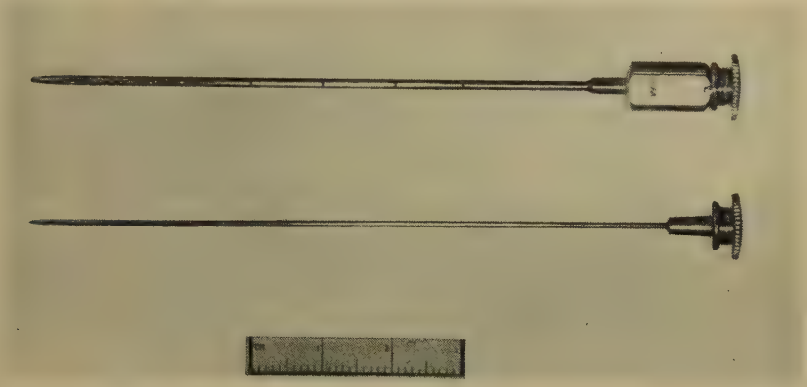


Fig. 689.—Brain Cannula with Trochar and blunt-ended Stylet. The Cannula is graduated in Centimetres.

very slightly outwards. The ventricle is usually reached when the cannula has penetrated about 3 cms. If the first attempt is unsuccessful it is important to withdraw the cannula completely before redirecting it to avoid slicing through the brain substance.

In the older child burr holes are usually drilled in the occipital region directly behind the posterior horn of the lateral fontanelle or in the frontal region over the anterior horn.

Subdural tap

This procedure is carried out when the existence of a subdural hæmatoma is suspected. The indications are fully discussed by Ingraham and Matson. In older children the skull must be drilled, but in infants the subdural space may be tapped through the lateral angles of the anterior fontanelle and in some cases further laterally through the coronal sutures. The scalp is prepared and the infant held as for ventricular puncture.

[1] The brain cannula may be obtained from Messrs. Willen Bros., 44 New Cavendish Street, London, W.1.

Lumbar puncture needles shortened to $\frac{1}{2}$ to $\frac{3}{4}$ inch, short-bevelled are used. The needle is first introduced at one lateral corner of the fontanelle or through the coronal suture at least 2 cm. from the midline at right angles to the surface of the skull (see fig. 690). The needle will be felt to pierce the dura almost immediately after transversing the skin. The stylet is

FIG. 690.—SUBDURAL TAP.

The needle is introduced at right angles to the skull in the right lateral angle of the anterior fontanelle. In this case no hæmatoma was found and cerebro-spinal fluid is seen dripping from the needle. The stylet is held in the left hand. The infant is securely wrapped and held and is sucking a teat containing cotton wool soaked in sugar water. Unless a strict no touch technique is to be employed, sterile rubber gloves must be worn.

then withdrawn and the operator waits, perhaps as much as two minutes, for fluid to emerge. In cases of subdural hæmatoma the fluid may be blood, altered blood, or yellow serum according to the age of the hæmatoma. Where there is no hæmatoma the dura mater and arachnoid will be in apposition and a few drops of clear cerebro-spinal fluid will appear. The puncture should then be repeated at the other lateral angle of the fontanelle and, if possible, half-way along the coronal sutures. In each case the needle must be directed at right angles to the surface.

Stomach Washout (Gastric Lavage)

This procedure may be helpful for:

(*a*) *Diagnostic purposes.*

(i) In a child with primary intra-thoracic tuberculosis to ascertain whether bacilli are being coughed up and swallowed.

(ii) To determine the quantity of residue in a vomiting infant suspected of pyloric stenosis.

(iii) To aid in the early diagnosis of congenital atresia of the œsophagus, in which the tube is arrested when about 10 cm. from the gum.

(*b*) As a *therapeutic measure* in, for instance, poisoning by ingestion and in pyloric stenosis treated medically.

(*c*) *Pre-operatively* to empty and clean the stomach before Rammstedt's operation for pyloric stenosis, or a gastro-jejunostomy for duodenal atresia or obstruction, or before laparotomy for other intestinal obstructions.

Sometimes the simple passage of a tube to relieve gaseous gastric distension of gas is useful.

Gastric lavage is surprisingly little upsetting to infants. It should be noted that thrush, if it is present in the mouth, may be caused to spread down the œsophagus, stomach and intestinal tract by the passage of instruments; inspection of the mouth will reveal the characteristic white patches and trans-oral instrumentation is withheld until the infection has cleared.

PROCEDURE.—An œsophageal tube with large enough bore to allow curds of the stomach contents to pass the lumen must be used (size 6 to 8 Eng. Cath. Gauge); smaller tubes will get blocked. Warm saline or water is preferable to even a weak sodium bicarbonate solution: alkalosis may already be pending and must not be encouraged. The tube is lubricated with a little saline solution and is simply slipped over the back of the tongue. Almost at once it is felt to be gripped by the muscles of deglutition and is easily passed down the œsophagus. There is little danger of inadvertently slipping the tube into the larynx, but it is wise to wait a minute or two with the tube in the œsophagus to ensure there is no to and fro air movement. A loud cry is reassuring. The tube passes the cardiac sphincter into the stomach with a characteristic plop. The residue is siphoned off and measured in a separate container. Then the funnel is attached to the tube and two or three ounces of fluid poured in; this is siphoned off and so on until the returns are clear, which is generally after about a pint of fluid has been used.

Œsophageal or Nasal Tube Feeding (Gavage)

When an infant is too weak to suck this can be an expedient measure. A tube can sometimes be passed through the nose with even less disturbance than through the mouth (size 6 to 8 Eng. Cath. Gauge). It will be remembered, however, that very young infants may not yet have learnt to breathe through their mouths so that the passage of a nasal tube and consequent blockage of that airway may cause alarming cyanosis and great embarrassment. The oral route will then be essential.

The feed is strained through muslin and given slowly with the tube far down the œsophagus or, probably better, right in the stomach. This feeding should not be resorted to more than four hourly Here again this procedure should not be instituted in the presence of thrush.

Passage of a Duodenal Tube

This may be necessary for :

(*a*) Cases of intestinal obstruction when continuous duodenal suction is desired.

(*b*) The collection of duodenal contents to estimate their enzyme content in suspected cases of cystic fibrosis of the pancreas. In the usual method of duodenal intubation for diagnostic purposes Levin's gastro-duodenal tube (opaque to X-ray, 6 to 8 English gauge) is helpful. It should be long enough to act as a siphon.

An estimate of the length of tube probably needed to enter the duodenum is marked by rough measurement against the child. The tube is passed through the nose. Stomach contents will first be withdrawn into a 10 or 20 c.cm. syringe ; these are practically always acid and usually colourless. When the duodenal contents are obtained they are bile stained and alkaline to litmus. Entrance into the duodenum may be a matter of some difficulty as the tube may curl back in the stomach.

First attempts should be made with the child lying on his right side, the tube being gently pushed onwards. If this is unsuccessful other positions should be tried, the child sitting up, leaning backwards or forwards or else lying on his face. It may be necessary to persist for an hour or more and success is sometimes achieved by leaving the child alone for half an hour with the tube stuck to his cheek at the estimated distance from the duodenum. X-ray screening, if available, is most useful as it enables the operator to be certain that the end of the tube lies in the pyloric region and the effect of attempts to assist its passage onwards may be observed. In addition, screening is necessary to confirm that the end of the tube is in the duodenum, when what appears to be duodenal juice is obtained ; in a lateral view the tube should be seen lying vertically just anterior to the spinal column. With the free end of the tube hanging below the level of the bed, duodenal juice will usually siphon over, but in cases of cystic fibrosis of the pancreas repeated suction may be required to obtain the viscid duodenal contents.

This procedure should be arranged for first thing in the morning, when nothing has been taken into the stomach since supper the night before. The juice is collected in tubes which are kept on ice.

A. H. James (1951) has devised an improved method which usually results in rapid duodenal intubation and which avoids the necessity of a long X-ray examination. In the end of the rubber tube is sealed a plug of a magnetic alloy. Its position in the stomach can thus be readily detected with the aid of a small pocket compass resting on the surface of the abdomen. The tube is passed through the nose with the aid of a wire introducer which is inserted through one of three eye-holes proximal to the metal plug. Once the end of the tube is through the nose the introducer is removed. As the tube reaches the cardia of the stomach the child is turned on to his face and in most instances the end of the tube will pass straight across the stomach towards the pylorus. The tube is passed into the stomach to within a few inches of the estimated length required

to reach the duodenum. The child is then rolled to face his left side and then over on to his back. The end of the tube is then located with the compass. If correctly placed, gentle massage is then applied over the pylorus whilst the tube is inserted a little further through the nose. Frequent use of the compass will control progress and trace the course of the end of the tube laterally and downwards.

Intramuscular Injections

The giving of intramuscular injections is frequently left to the nursing staff. It is advisable that insistence is made on only the safest site being allowed. The gluteal region of infants is small and the upper outer quadrant is therefore not far from the sciatic nerve ; the whole region may be frequently soiled and wet. The deltoid region is even smaller so that vessels and nerves are not far distant ; also the deltoid bursa may be inadvertently entered, and if this communicates with the shoulder joint capsule dire results may ensue. A septic arthritis in an infant has actually been seen following a deltoid " intramuscular " injection. The outer aspect of the thigh into the vastus externus muscle is the best site. This area does not contain any important nerves or large blood vessels. Alternatively the area immediately above the greater trocanter and below the iliac crest fulfils the necessary conditions.

Artificial Respiration

When artificial respiration is required, more than re-ventilation of the lungs will be necessary. Resuscitation is a matter of ventilation and treatment of shock : the establishment of respiration, circulation and maintenance of warmth. Sudden need for artificial respiration may occur during anæsthesia, smothering by bed-clothes, such accidents as drowning, electric shock and suffocation from smoke or gases as well as from conditions of paralysis such as diphtheritic, anterior poliomyelitic, or tetanic.

When asphyxia occurs as an acute emergency no time should elapse before some method of artificial respiration is started and Schafer's method can be started until the rocking method can be instituted. It is interesting to note that Eve's method of rocking was first employed in 1932 for a case of diphtheritic diaphragmatic paralysis in a child ; it was not popularized, however, until the recent war years.

Procedure.—The patient is placed on a flat surface supported on a fulcrum, for instance a board under a mattress on a stool, and rocked through a total angle of sixty to ninety degrees 20 to 30 double rocks a minute (12 to 15 double rocks per minute had been recommended for adults, though lately a faster rate has been proposed). The first rock should be head down at an angle of forty-five degrees.

A baby may be rocked at once in the arms of a doctor or nurse.

There is always a greater or lesser element of shock and circulatory failure associated with the respiratory failure ; for these the rocking method has more to recommend it than either Schafer's or Silvester's methods of artificial respiration :

(*a*) The patient is at rest and can be kept covered and warm.
(*b*) It is harmless: the ribs and viscera cannot be injured.
(*c*) Lung ventilation figures for various methods by different observers vary considerably, but the rocking method would seem to give as good, if not better, tidal air flow results.
(*d*) It is simple and not tiring and requires no skill.

Oxygen should be administered through a nasal catheter or a B.L.B. mask, or better still through a close-fitting anæsthetic mask.

The circulation may be further stimulated by giving 1 c.cm. nikethamide intramuscularly or intravenously.

Mechanical respirators.—Mechanical respirators are necessary for prolonged artificial respiration. The Both box respirator is most commonly used in British hospitals.

INDICATIONS.—(1) Spinal poliomyelitis with involvement of diaphragm and/or intercostal muscles. (Although mechanical artificial respiration may have to be used in cases of bulbar poliomyelitis involving the respiratory centres, it is unlikely to be effective. In cases of bulbar poliomyelitis with pharyngeal paralysis its use is contraindicated, unless severe diaphragmatic or intercostal paralysis co-exists. In these circumstances its use may be imperative, but assiduous pharyngeal aspiration or tracheotomy will be necessary.)

(2) Post-diphtheritic respiratory paralysis.
(3) Infective polyneuritis.
(4) Acute poisoning (barbiturates, carbon monoxide).

Children with spinal poliomyelitis should be placed in the respirator at the first sign of respiratory muscle paralysis or if there is a weakness of the sternomastoid or deltoid muscles, which suggest that diaphragmatic paralysis is imminent. When there is already severe respiratory paralysis, such relief will be felt by the child when he is placed in the respirator, that he will forget to be frightened. In cases of milder or early paralysis, however, the child may be terrified. It may then be possible to place him in the respirator, which is left open, while he becomes used to his surroundings. If this is not possible a sedative must be given, bearing in mind that heavy sedation will increase the risk of pneumonia.

The best collars are of sponge rubber and equipped with a zip fastener. They should not fit too tightly round the neck as the inevitable to and fro movements may cause severe abrasions. The space between the collar and neck should be filled with cotton wool or layers of lint and the skin protected by a suitable cream. The clothing must be light, easily removable and must not encircle the neck. Woollen stockings will protect the legs from cold due to the influx of air.

The *respiratory rate* should be between 20 and 30 per minute and will have to be carefully adjusted to synchronize with the child's own respiratory efforts.

The *pressure* is measured on a water manometer and is the distance between the levels of water in the limbs of the U-tube at their maximum excursion. In the Both respirator only one limb of the U-tube is visible, but the scale attached is reduced by one half, so that a distance of say

5 cm. is marked 10 cm. –giving the correct negative pressure. Negative pressures of over 15 cm. of water are liable to produce pulmonary emphysema and in practice the pressure is kept as low as possible compatible with adequate ventilation. Wilson (1947) recommends holding a stethoscope over the mouth and nose of the sleeping child, whilst adjusting the pressure. If the negative pressure is too high, stridor will be heard due to involuntary partial closure of the glottis on inspiration. If the pressure is too low, extra respiratory efforts, movements of the alæ nasæ or twitching of the mouth will be observed. A negative pressure of 10 to 12 cm. of water is usually satisfactory.

It is generally advisable to tilt the patient head down by 15° to 20° to reduce the chances of aspiration of secretions from the mouth and throat. The sucking out of these secretions becomes, of course, of vital importance when there is pharyngeal paralysis.

Feeding may be difficult at first, but the patient usually learns quickly to time his swallowing with the rhythm of the machine. Constipation may be combatted by giving a daily laxative.

One nurse must always be present and two or three are necessary for any nursing procedure, to reduce the time that the patient is out of the respirator. Changes of position should be made several times a day and the pressure points protected against sores. All attendants on the patient and all visitors must wear face masks to lessen the chances of fatal respiratory infection.

A Perspex shelf, fitted over the head of the patient, on which a book may be placed page downwards, a mirror or even, where possible, an epidiascope will help to keep the child amused. Finally it must be remembered that patients tire easily out of the respirator and therefore examination by the doctor should be as rapid as possible.

In cases of poliomyelitis the child must be kept in the respirator at least until the temperature is normal and the muscle tenderness has disappeared. His removal from the apparatus must be an intermittent and gradual process.

Sarnoff (1950) has used electrophrenic stimulation successfully in a case of bulbar poliomyelitis with central respiration failure. He originally exposed the phrenic nerve and attached the electrode to it, but equally successful stimulation has since been achieved with skin electrodes (Sarnoff *et al.*, 1951).

Asphyxia neonatorum.—Gentle handling is all important and has replaced violent methods of peripheral stimulation and artificial respiration. The infant should be wrapped in a warmed blanket, the head rather lower than the feet. It is essential first to empty the air passages of mucus and aspirated amniotic fluid. This is best carried out by direct intubation through a small laryngoscope, but this method requires skill which may not always be available. Therefore the mucus catheter is most commonly used for this purpose and is indeed quite effective. Lobeline hydrochloride $\frac{1}{20}$ grain may be injected into the umbilical vein in the hope that it will stimulate circulation and respiration. It is as well that the injection should be made by someone capable of distinguishing the umbilical vein

from the umbilical arteries in a shocked infant as accidental arterial injection of lobeline has been thought to be responsible for arterial lesions and occasionally paralyses in the lower limbs of newborn infants (Mills, 1949). Oxygen blown through a funnel on to the face may provide the skin stimulus necessary to initiate respiration, but it is not a very effective method of administering oxygen which is best given through a baby's anæsthetic mask. If the infant does not breathe after the air passages have been cleared of secretions, some form of artificial respiration must be used. Rocking or intermittent manual compression of the lower chest may be effective in mild cases of asphyxia. Insufflation of the lungs by positive pressure can be dangerous unless carefully controlled and in serious cases the most effective and least dangerous method of artificial respiration is electrophrenic stimulation. This procedure, re-introduced by Sarnoff and his colleagues in 1948, has been adapted for use in asphyxia neonatorum by Cross. It has the advantages that it allows minimum handling of the infant and normal intrathoracic pressures.

The apparatus,[1] which needs a main electricity supply, produces intermittent faradic stimuli devised to mimic potential changes in the phrenic nerve during normal respiration. The frequency is fixed at 18 per minute, but the strength of the current can be adjusted.

It is essential to clear the upper respiratory tract of mucus before beginning the stimulation. The indifferent electrode—a metal plate covered with lint soaked in saturated saline solution—is placed under the infant. The active electrode—a silver-plated probe also covered with wet lint—is placed firmly over the motor point of one phrenic nerve. With the infant's head turned to the opposite side, this point is located just behind the sterno-mastoid muscle at the junction of its middle and lower thirds. The electrode may have to be moved slightly to find its most effective position. The current is then increased until contraction of the diaphragm is revealed by movements of the upper abdomen or by breath sounds heard on auscultation. In general the more severely asphyxiated the baby, the larger will be the current needed to produce contractions of the diaphragm. During the precedure oxygen should be administered. Stimulation should be continued until the infant breathes spontaneously or until five minutes after the heart action ceases. Recovery has taken place in an apparently moribund infant after as long as four hours' stimulation of the phrenic nerve.

If this apparatus is not available and if simple methods have been unsuccessful, positive pressure artificial respiration should be applied, as for instance with the aid of a rubber bag fitted to the anæsthetic mask (O'Donel Browne, 1950). The positive pressure should never exceed 12 to 15 cm. of water. Alternatively tracheal intubation, as described by Blaikley and Gibberd (1935), may be adopted. In desperate cases very gentle mouth to mouth insufflation is justifiable, if more controlled methods are not available.

Babies with partial atelectasis with repeated attacks of cyanosis are

[1] The " Stanco " Phrenic Nerve Stimulator, Stanley Cox, Ltd., 11 Gerrard Street, London, W.1.

best nursed in an oxygen box or incubator with a continuous supply of oxygen, which should not be allowed to rise above 40 per cent. In practice the flow should be adjusted so that cyanosis is just abolished and the percentage of oxygen in the inspired air should be lowered gradually before the infant finally leaves the incubator.

Five per cent. carbon dioxide may be added hourly or two-hourly to ensure that they have at least ten deep breaths. If the atelectasis is confined to one side it is wise to let the baby lie on the opposite side.

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